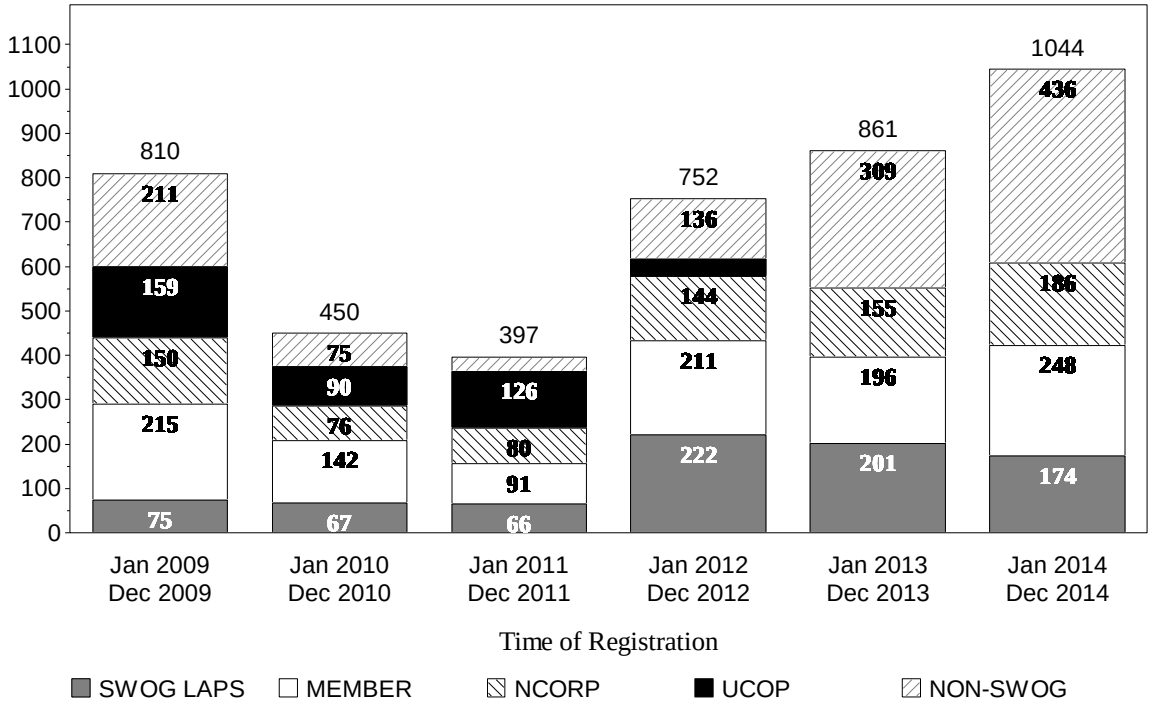
GENITOURINARY COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
GENITOURINARY COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

GENITOURINARY COMMITTEE

	Jul 2014 Dec 2014	Jan 2014 Jun 2014	Jul 2013 Dec 2013	All Patients
S0931 Renal, EVEREST				
Randomization				
Blinded drugs	205	173	178	1,014
S1011 Blad, Standard vs Extended LND				
Initial registration				
Pre-surgical registration	74	61	75	421
Randomization				
Standard LND	37	26	40	200
Extended LND	36	27	35	196
	73	53	75	396
S1014 Pros, Mets, Abi Acetate				
Registration				
Abiraterone Acetate	0	0	4	41
S1107 Renal, Adv, ARQ 197 +/- Erlo				
Randomization				
ARQ 197	0	0	10	27
ARQ 197 + Erlotinib	0	0	12	28
	0	0	22	55
S1216 Pros Adv, ADT +/- TAK-700 or Bic				
Randomization				
LHRHa + TAK-700	86	114	74	291
LHRHa + Bicalutamide	87	109	78	292
	173	223	152	583
S1314 Blad, COXEN Neoadj. Chemo + Cyst				
Registration/Randomization				
GC+CYST	1	0	0	1
DDMVAC+CYST	2	0	0	2
	3	0	0	3

	Jul 2014 Dec 2014	Jan 2014 Jun 2014	Jul 2013 Dec 2013	All Patients
A031201 CRMPC, Enza +/- (Abira + Predni)*				
Total Registrations	31	13	0	44
C70807 Pros, MEAL Study*				
Total Registrations	26	23	21	134
C90203 Pros, Surgery +/- Neoadj Chemo*				
Total Registrations	7	3	12	145
C90601 Trans cell, blind bev vs placebo*				
Total Registrations	7	9	11	100
E2810 Renal, Pazopanib vs Placebo*				
Total Registrations	1	9	7	23
R0534 Pros, PBRT +/- NC-STAD +/- PLNRT*				
Total Registrations	3	0	0	3
R0815 Pros, dose-esca. RT +/- ADT*				
Total Registrations	2	3	1	6
R0924 Pros, NADT+WPRT vs NADT+P&SV RT*				
Total Registrations	2	0	1	3
R1115 Pros, (ADT + RT) +/- TAK-700*				
Total Registrations	0	1	1	2

* For non-SWOG coordinated studies only SWOG registrations are shown.

S0931 Phase III

Coordinating Group: SWOG

EVEREST: EVErolimus for Renal Cancer Ensuing Surgical Therapy, a Phase III Study

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Participants:
SWOG, CTSU (supported by Alliance, ECOG-ACRIN)

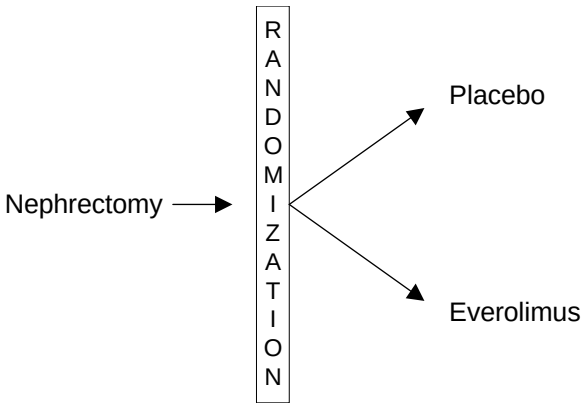
Date Activated:
04/01/2011

Study Chairs:
C Ryan, E Heath, P Lara, G Palapattu, P Mack

Statisticians:
C Tangen, M Plets

Data Coordinator:
A Hamm

SCHEMA



Objectives

To compare recurrence-free survival in renal carcinoma patients randomly assigned to one year of everolimus versus one year of placebo after nephrectomy or partial nephrectomy.

To compare overall survival in those patients randomized to everolimus versus those randomized to placebo.

To compare qualitative and quantitative toxicity between the two study arms.

To collect tissue and biologic specimens for molecular biomarkers relevant to the AKT/mTOR and other pathways implicated in the pathogenesis of renal carcinoma and to investigate their potential predictive and prognostic value.

To investigate the relationship between steady state trough levels of everolimus and relevant side effects (lymphopenia, infection, hyperglycemia, hypercholesterolemia, hypertriglyceridemia) in patients treated on this study with everolimus.

Patient Population

Patients must have histologically or cytologically confirmed renal cell carcinoma (collecting duct or medullary carcinomas excluded). Patients must be considered pathologically either Intermediate High Risk or Very High Risk as defined in the protocol. Patients must not have a history of distant metastases. Patients with microvascular invasion of the renal vein of any grade or stage (provided they are M0) are also eligible. Patients must not have any evidence of residual or metastatic renal cell cancer on CT scan of the chest, abdomen, and pelvis after nephrectomy and within a maximum of 28 days prior to registration.

Patients must have undergone a full surgical resection (radical nephrectomy or partial nephrectomy), including removal of all clinically positive nodes. Surgical margins must be negative. Patients with positive renal vein margins are eligible unless there is invasion of the renal vein wall at the margin (provided no other margins are positive). Patients must plan to start study drug within 84 days after the date of full surgical resection. Patients must have recovered from any surgical-related complications.

Patients must not have received any prior anti-cancer therapy (except for radical or partial nephrectomy noted above) for renal cell carcinoma, including systemic therapy in the adjuvant or neoadjuvant setting, immunotherapy, investigational therapy, surgical metastasectomy, or radiation therapy. Patients must not be planning to receive other anti-cancer agents including investigational agents during the period on study.

Patients must have a Zubrod performance status of 0 or 1. Patients must have adequate cardiac, pulmonary, renal, hepatic, and hematologic function. Patients must not be taking strong CYP3A4 inhibitors or inducers within 14 days prior to randomization nor planning to take during the course of protocol therapy. Patients must not have any known hypersensitivity to everolimus, other rapamycins (sirolimus, temsirolimus), or its excipients. Patients must be able to take oral medications. Patients must be offered the opportunity to participate in the translational medicine studies.

Stratification/Descriptive Factors

Treatment randomization will be stratified according to the following factors: (1) risk group based on pathologic stage: intermediate high risk vs very high risk; (2) histology: clear cell vs non-clear cell; and (3) performance status: 0 vs 1.

Accrual Goals

The accrual goal for this study is 1,170 eligible patients. Four interim analyses will be performed when there is 30%, 50%, 70%, and 90% information.

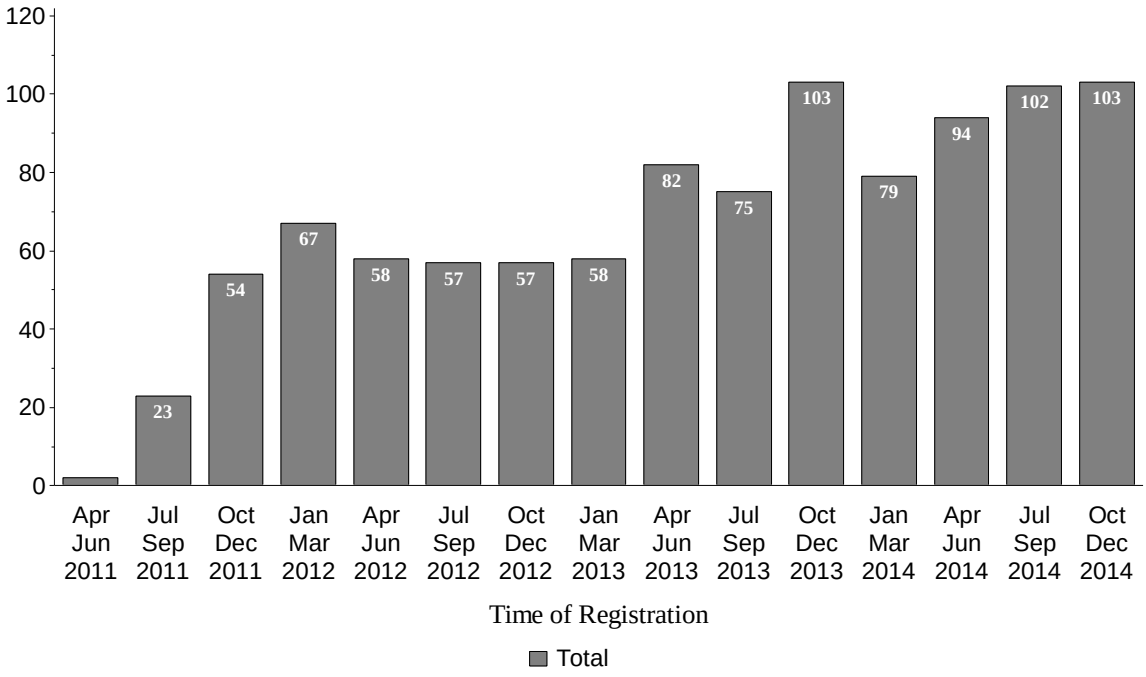
Summary Statement

As of December 31, 2014, 1014 patients had been registered to this study. It was anticipated that 28 patients per month (336 per year) would be randomized to this study and that target has been reached over the past six months. One hundred four patients are currently ineligible, including 81 patients with insufficient baseline documentation, of which 45 are potentially reversible. Insufficient baseline documentation is primarily due to CT scan or lab tests not done or completed outside of the allowable window. Major deviations are coded for 11 patients, who received no protocol treatment; these 11 patients are not assessable for adverse events. One additional patient was removed from protocol treatment after only two days of study drug due to positive surgical margins and is not assessable for adverse events.

Eight hundred sixty patients have been assessed for adverse events. Sixteen patients experienced Grade 4 toxicities, seven with hypertriglyceridemia; one with multi-organ failure and acute renal injury coded as "Renal/urinary disorders-Other"; another with multi-organ failure, increased creatinine and acidosis; one with thromboembolic event; one with anemia; one with increased ALT and AST; one with mucositis oral; one with hyperuricemia; one with dyspnea; and one with lymphopenia. Two hundred fourteen patients in the pooled treatment arms experienced Grade 3 toxicities as maximum degree, primarily oral mucositis (63), hypertriglyceridemia (41), hyperglycemia (23), fatigue (21), hypertension (21), and rash acneiform (11). Additional Grade 3 toxicities include: one patient with congestive heart failure coded as “Cardiac disorder-Other”; one patient with a campylobacter infection and one patient with influenza B, both coded as “Infections/infestations-Other”; one with a transient neurological deficit coded as “Nervous sys disorders-Other”; one with stomatitis coded as “GI disorders-Other”; and one with central retinal vein occlusion coded as “Eye disorders-Other”. No Grade 5 toxicities have been reported.

Due to a larger drop out rate than originally anticipated, this study is currently in the process of being amended to sizably increase the accrual goal.

Initial Registrations By 3 Month Intervals



Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
ECOG-ACRIN	258	Davis, U of CA	9
Alliance	198	Hawaii MU-NCORP	9
NRG	39	Wayne State Univ	9
City of Hope Med Ctr	25	Cedars-Sinai Med Ctr	8
Southeast CCC NCORP	23	Atlanta Reg CCOP	7
Michigan, U of	20	Montana NCORP	7
Heartland NCORP	17	Nevada CRF NCORP	7
Loyola University	17	Oregon Hlth Sci Univ	7
Michigan CRC NCORP	16	PCRC NCORP	7
Sutter General Hosp/Sutter Cancer RC	16	West Michigan NCORP	7
Utah, U of	16	Carolinas Med Ctr/San Antonio, U of TX	6
Baylor College	15	Columbia MU-NCORP	6
Kansas, U of	14	Virginia Mason MC/Northwest NCORP	6
Dayton NCORP	13	Greenville NCORP	5
Wichita NCORP	13	Kansas City NCORP	5
Columbus NCORP	12	Poudre Valley Hosp/Colorado, U of	5
Colorado, U of	11	So Calif, U of	5
Rochester, Univ of	11	St Jude Medical Ctr/Irvine, U of CA	5
San Antonio, U of TX	11	Utah, U of - UCOP/Utah, U of	5
Gulf South MU-NCORP	10	All Other Institutions	115
Ozarks Reg NCORP	10	**Total (95 Institutions)**	**1014**
Arizona MC, U of	9		

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2014; Data as of February 5, 2015

	Total
NUMBER REGISTERED	1014
INELIGIBLE	104
Insufficient Documentation	81
Irreversible	36
Reversible	45
ELIGIBLE	910
Analyzable, Pend. Elig.	153
ADVERSE EVENT ASSESSMENT	
Evaluable	860
Not Evaluable	12
Too Early	38

Patient Characteristics

Registrations ending December 31, 2014; Data as of February 5, 2015

	Total (n=910)	
AGE		
Median	57.9	
Minimum	18.1	
Maximum	90.0	
SEX		
Males	627	69%
Females	283	31%
HISPANIC		
Yes	61	7%
No	825	91%
Unknown	24	3%
RACE		
White	817	90%
Black	41	5%
Asian	22	2%
Pacific Islander	1	0%
Native American	7	1%
Multi-Racial	2	0%
Unknown	20	2%

	Total (n=910)	
RISK GROUP		
Intermediate High	421	46%
Very High	489	54%
HISTOLOGY		
Clear Cell (any component)	760	84%
Non-Clear Cell	150	16%
PERFORMANCE STATUS		
0	729	80%
1	181	20%

Treatment Summary

Registrations ending December 31, 2014; Data as of February 5, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	267
NUMBER OFF PROTOCOL TREATMENT	643
REASON OFF TREATMENT	
Treatment completed as planned	306
Adverse Event or side effects	177
Refusal unrelated to adverse event	37
Progression/relapse	95
Death	0
Other - not protocol specified	22
Reason under review	6
MAJOR PROTOCOL DEVIATIONS	11

Number of Patients with a Given Type and Grade of Adverse Event

Combined Blinded Treatment Arms

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2014; Data as of February 5, 2015

ADVERSE EVENT	Total (n=860) Grade 0	1	2	3	4	5
ALT increased	761	88	8	2	1	0
AST increased	764	86	6	3	1	0
Abdominal distension	858	1	1	0	0	0
Abdominal infection	859	0	0	1	0	0
Abdominal pain	798	43	14	5	0	0
Acidosis	859	0	0	0	1	0
Acute kidney injury	857	2	1	0	0	0
Agitation	858	1	0	1	0	0
Alkaline phosphatase increased	795	64	1	0	0	0
Allergic reaction	857	2	0	1	0	0
Allergic rhinitis	855	5	0	0	0	0
Alopecia	844	16	0	0	0	0
Anal fistula	859	0	1	0	0	0
Anal mucositis	858	1	1	0	0	0
Anal pain	859	1	0	0	0	0
Anemia	633	196	24	6	1	0
Anorexia	773	61	25	1	0	0
Anxiety	852	8	0	0	0	0
Arthralgia	810	41	8	1	0	0
Arthritis	859	1	0	0	0	0
Ataxia	859	0	1	0	0	0
Back pain	846	10	3	1	0	0
Bladder infection	859	0	1	0	0	0
Bloating	852	7	1	0	0	0
Blood bilirubin increased	835	23	2	0	0	0
Blood gonadotrophin abnormal	859	1	0	0	0	0
Blood/lymph disorder-Other	856	3	1	0	0	0
Blurred vision	851	7	2	0	0	0
Bone infection	859	0	0	1	0	0
Bone pain	852	7	1	0	0	0
Breast infection	859	0	1	0	0	0
Breast pain	859	1	0	0	0	0
Bronchial infection	856	0	4	0	0	0
Bronchopulmonary hemorrhage	858	2	0	0	0	0
Bruising	857	3	0	0	0	0
Bullous dermatitis	858	1	0	1	0	0
CD4 lymphocytes decreased	854	5	1	0	0	0
CPK increased	855	3	2	0	0	0
Cardiac disorder-Other, spec	858	1	0	1	0	0
Cardiac troponin I increased	859	1	0	0	0	0
Cheilitis	859	0	1	0	0	0
Chest pain - cardiac	858	2	0	0	0	0
Chest wall pain	858	1	1	0	0	0
Chills	838	22	0	0	0	0
Cholesterol high	580	231	47	2	0	0
Chronic kidney disease	852	2	4	2	0	0
Cognitive disturbance	858	2	0	0	0	0
Colitis	858	0	1	1	0	0
Concentration impairment	857	3	0	0	0	0
Confusion	858	2	0	0	0	0
Conjunctivitis	859	1	0	0	0	0
Constipation	819	38	3	0	0	0
Cough	773	70	17	0	0	0
Creatinine increased	655	167	35	2	1	0
Dehydration	842	3	7	8	0	0
Dental caries	858	1	1	0	0	0
Depression	853	6	1	0	0	0
Dermatitis radiation	856	3	1	0	0	0
Diarrhea	661	153	36	10	0	0
Dizziness	803	51	5	1	0	0
Dry eye	849	11	0	0	0	0
Dry mouth	806	53	1	0	0	0
Dry skin	757	82	16	5	0	0
Dysesthesia	858	1	1	0	0	0
Dysgeusia	763	81	16	0	0	0
Dyspepsia	840	14	6	0	0	0
Dysphagia	855	5	0	0	0	0
Dysphasia	859	1	0	0	0	0
Dyspnea	764	63	27	5	1	0
Ear pain	857	3	0	0	0	0
Ear/labyrinth disorders-Other	859	1	0	0	0	0
Edema face	852	7	1	0	0	0
Edema limbs	789	59	11	1	0	0
Edema trunk	859	1	0	0	0	0
Endocarditis infective	859	0	0	1	0	0
Endocrine disorders-Other	857	3	0	0	0	0
Enterocolitis	859	0	1	0	0	0
Epistaxis	806	50	4	0	0	0
Erectile dysfunction	857	2	1	0	0	0
Erythema multiforme	832	22	6	0	0	0
Esophageal pain	859	1	0	0	0	0
Esophagitis	856	1	3	0	0	0
Eye disorders - Other, specify	855	4	0	1	0	0
Eye infection	857	0	3	0	0	0
Eye pain	857	2	1	0	0	0
Eyelid function disorder	859	1	0	0	0	0
FEV1 decreased	859	0	1	0	0	0
Facial pain	859	1	0	0	0	0

ADVERSE EVENT	Total (n=860) Grade 0	1	2	3	4	5
Fatigue	451	286	102	21	0	0
Fever	841	17	2	0	0	0
Flank pain	854	3	3	0	0	0
Flatulence	850	9	1	0	0	0
Flu like symptoms	854	6	0	0	0	0
Flushing	851	9	0	0	0	0
GERD	855	4	1	0	0	0
GGT increased	859	1	0	0	0	0
GI disorders-Other, specify	842	13	4	1	0	0
Gastric hemorrhage	859	0	1	0	0	0
Gastritis	859	0	0	1	0	0
Gastrointestinal pain	858	2	0	0	0	0
Gen disorders/admin site cond	852	6	2	0	0	0
Generalized muscle weakness	839	19	2	0	0	0
Gingival pain	857	3	0	0	0	0
Glucose intolerance	855	3	1	1	0	0
Gum infection	859	0	1	0	0	0
Hand-Foot syndrome	846	6	8	0	0	0
Headache	742	98	18	2	0	0
Heart failure	858	0	0	2	0	0
Hematuria	854	5	1	0	0	0
Hemoglobin increased	857	3	0	0	0	0
Hemorrhoidal hemorrhage	858	2	0	0	0	0
Hemorrhoids	853	4	2	1	0	0
Hoarseness	858	2	0	0	0	0
Hot flashes	849	9	2	0	0	0
Hypercalcemia	853	7	0	0	0	0
Hyperglycemia	614	171	52	23	0	0
Hyperhidrosis	858	2	0	0	0	0
Hyperkalemia	843	12	4	1	0	0
Hypernatremia	855	5	0	0	0	0
Hypersomnia	859	1	0	0	0	0
Hypertension	771	25	43	21	0	0
Hypertriglyceridemia	513	199	100	41	7	0
Hyperuricemia	852	7	0	0	1	0
Hypoalbuminemia	846	14	0	0	0	0
Hypocalcemia	832	26	2	0	0	0
Hypoglycemia	856	3	1	0	0	0
Hypokalemia	847	13	0	0	0	0
Hypomagnesemia	853	7	0	0	0	0
Hyponatremia	848	11	0	1	0	0
Hypophosphatemia	851	4	3	2	0	0
Hypotension	856	2	2	0	0	0
Hypothyroidism	859	1	0	0	0	0
Infections/infestations-Other	847	4	7	2	0	0
Injection site reaction	859	1	0	0	0	0
Insomnia	829	26	5	0	0	0
Investigations-Other, specify	847	11	2	0	0	0
Irregular menstruation	859	1	0	0	0	0
Irritability	858	1	0	1	0	0
Laryngeal inflammation	858	2	0	0	0	0
Laryngeal mucositis	859	0	0	1	0	0
Lethargy	859	0	1	0	0	0
Leukocytosis	859	0	0	1	0	0
Libido decreased	857	3	0	0	0	0
Lip infection	854	5	1	0	0	0
Lip pain	857	2	1	0	0	0
Localized edema	856	4	0	0	0	0
Lung infection	847	0	8	5	0	0
Lymphedema	859	1	0	0	0	0
Lymphocyte count decreased	811	38	9	1	1	0
Lymphocyte count increased	859	0	1	0	0	0
MS/connective tissue disorder	856	4	0	0	0	0
Malaise	853	6	1	0	0	0
Memory impairment	857	3	0	0	0	0
Metab/nutrition disorders-Oth	852	7	1	0	0	0
Movements involuntary	858	2	0	0	0	0
Mucosal infection	856	2	2	0	0	0
Mucositis oral	514	186	96	63	1	0
Multi-organ failure	858	0	0	0	2	0
Muscle weakness lower limb	859	1	0	0	0	0
Muscle weakness right-sided	859	1	0	0	0	0
Muscle weakness upper limb	859	1	0	0	0	0
Myalgia	812	37	11	0	0	0
Myocardial infarction	859	0	0	1	0	0
Myositis	859	1	0	0	0	0
Nail discoloration	853	7	0	0	0	0
Nail infection	859	1	0	0	0	0
Nail loss	851	8	1	0	0	0
Nail ridging	848	12	0	0	0	0
Nasal congestion	842	13	5	0	0	0
Nausea	696	130	32	2	0	0
Neck pain	854	5	1	0	0	0
Neoplasms, all	859	0	1	0	0	0
Nervous sys disorders-Other	859	0	0	1	0	0
Neutrophil count decreased	818	27	12	3	0	0
Non-cardiac chest pain	850	6	1	3	0	0
Obesity	859	0	0	1	0	0
Obstruction gastric	859	0	0	1	0	0
Oral dysesthesia	856	4	0	0	0	0
Oral hemorrhage	858	2	0	0	0	0
Oral pain	839	14	7	0	0	0
Otitis externa	859	0	1	0	0	0
Pain	837	19	3	1	0	0
Pain in extremity	840	15	4	1	0	0
Pain of skin	851	9	0	0	0	0
Palpitations	853	6	1	0	0	0
Papulopustular rash	852	7	1	0	0	0
Paresthesia	853	7	0	0	0	0
Paronychia	857	2	1	0	0	0
Pelvic pain	858	2	0	0	0	0
Pericardial effusion	859	0	1	0	0	0

ADVERSE EVENT	Total (n=860) Grade 0	1	2	3	4	5
Periodontal disease	859	1	0	0	0	0
Periorbital edema	856	4	0	0	0	0
Peripheral motor neuropathy	857	1	2	0	0	0
Peripheral sensory neuropathy	836	18	6	0	0	0
Pharyngeal mucositis	857	2	1	0	0	0
Pharyngitis	858	0	2	0	0	0
Pharyngolaryngeal pain	859	1	0	0	0	0
Photosensitivity	854	5	0	1	0	0
Platelet count decreased	775	83	2	0	0	0
Pneumonitis	819	15	23	3	0	0
Postnasal drip	857	2	1	0	0	0
Productive cough	854	4	2	0	0	0
Proteinuria	856	4	0	0	0	0
Pruritus	761	75	19	5	0	0
Psych disorders-Other, spec	859	0	1	0	0	0
Purpura	855	4	1	0	0	0
ROM decreased	859	1	0	0	0	0
Rash acneiform	715	114	20	11	0	0
Rash maculo-papular	707	111	33	9	0	0
Rash pustular	859	0	1	0	0	0
Rectal mucositis	857	3	0	0	0	0
Rectal pain	859	1	0	0	0	0
Renal/urinary disorders-Other	853	6	0	0	1	0
Resp/thoracic/mediastinal ds	854	4	1	1	0	0
Restlessness	859	1	0	0	0	0
Rhinitis infective	857	0	3	0	0	0
Scalp pain	858	2	0	0	0	0
Seroma	859	0	0	1	0	0
Sinus bradycardia	858	2	0	0	0	0
Sinus disorder	858	2	0	0	0	0
Sinus pain	859	1	0	0	0	0
Sinus tachycardia	855	4	1	0	0	0
Sinusitis	855	0	5	0	0	0
Skin hyperpigmentation	858	2	0	0	0	0
Skin hypopigmentation	858	2	0	0	0	0
Skin infection	847	2	10	1	0	0
Skin ulceration	859	1	0	0	0	0
Skin/subq tissue ds-Other	823	32	5	0	0	0

ADVERSE EVENT	Total (n=860) Grade 0	1	2	3	4	5
Soft tissue infection	859	0	0	1	0	0
Somnolence	857	3	0	0	0	0
Sore throat	826	30	4	0	0	0
Stomach pain	854	6	0	0	0	0
Stomal ulcer	859	0	1	0	0	0
Syncope	859	0	0	1	0	0
Testicular disorder	859	1	0	0	0	0
Testicular pain	859	0	1	0	0	0
Thromboembolic event	858	0	0	1	1	0
Tinnitus	853	7	0	0	0	0
Tooth infection	858	0	1	1	0	0
Toothache	857	2	1	0	0	0
Transient ischemic attacks	859	0	1	0	0	0
Tremor	858	2	0	0	0	0
Upper respiratory infection	853	0	6	1	0	0
Urinary frequency	853	6	1	0	0	0
Urinary incontinence	857	3	0	0	0	0
Urinary retention	858	1	1	0	0	0
Urinary tract infection	850	0	8	2	0	0
Urinary urgency	859	1	0	0	0	0
Urticaria	857	2	1	0	0	0
Vaginal discharge	858	1	1	0	0	0
Vaginal hemorrhage	859	1	0	0	0	0
Vaginal infection	859	0	1	0	0	0
Vasc disorders-Other, spec	859	1	0	0	0	0
Vertigo	857	3	0	0	0	0
Vital capacity abnormal	859	1	0	0	0	0
Voice alteration	858	2	0	0	0	0
Vomiting	807	34	16	3	0	0
Watering eyes	851	9	0	0	0	0
Weight gain	847	9	3	1	0	0
Weight loss	829	29	2	0	0	0
Wheezing	859	1	0	0	0	0
White blood cell decreased	781	70	9	0	0	0
Wound complication	859	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	113	218	299	214	16	0

S1011 Phase III

Coordinating Group: SWOG

A Phase III Surgical Trial to Evaluate the Benefit of a Standard versus an Extended Pelvic Lymphadenectomy Performed at Time of Radical Cystectomy for Muscle Invasive Urothelial Cancer

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Participants:
SWOG, CTSU (supported by Alliance, ECOG-ACRIN, NCIC CTG)

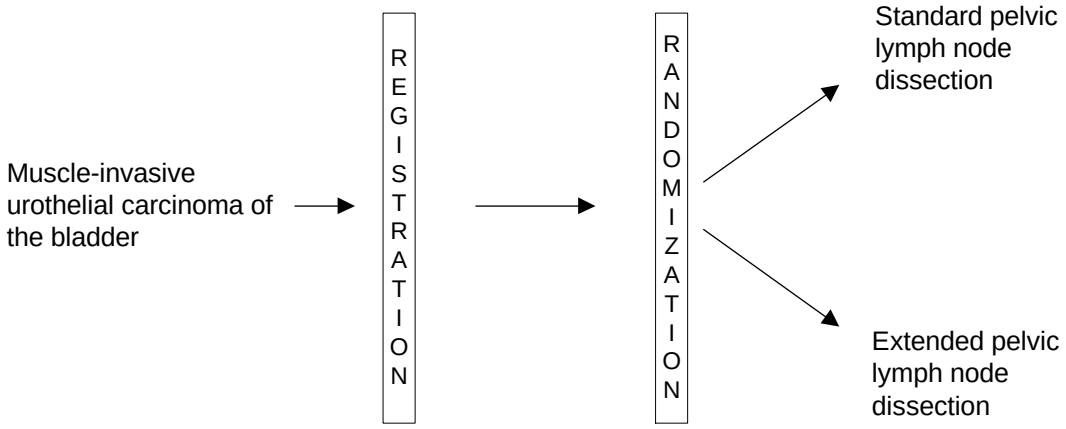
Date Activated:
08/01/2011

Study Chairs:
S Lerner, T Koppie, R Svatek, A Alva

Statisticians:
C Tangen, M Plets

Data Coordinator:
J Barce

SCHEMA



Objectives

To compare disease-free survival (DFS) in patients undergoing radical cystectomy for muscle-invasive urothelial carcinoma of the bladder treated with radical cystectomy and extended pelvic lymph node dissection compared to radical cystectomy and standard pelvic lymphadenectomy.

To compare overall survival (OS) in the two study arms.

To evaluate operative time; whether or not nerve sparing was performed; intra-operative; peri-operative; and 90-day morbidity and mortality; length of hospital stay; histology (pure urothelial versus mixed); lymph node counts and lymph node density; adjuvant chemotherapy received; and local and retroperitoneal soft tissue recurrence in the two study arms.

To collect paraffin embedded blocks for translational medicine studies including markers of epithelial and messenchymal transition and correlate these findings with pathologic T stage and node metastasis as well as DFS and OS.

Patient Population

Patients must have histologically proven T2, T3, or T4a urothelial carcinoma of the bladder that requires primary radical cystectomy for definitive treatment. There must be plans for the cystectomy and lymph node dissection to be performed within 28 calendar days following registration. Laparoscopic surgery is not allowed. Patients must have no evidence of visceral or nodal metastatic disease proximal to the common iliac bifurcation.

Patients must not have undergone a prior partial cystectomy for invasive bladder cancer. Patients must not have received any prior pelvic surgery that would obviate a complete extended lymphadenectomy. Prior neoadjuvant chemotherapy for this cancer is permitted however patients must have completed treatment within 70 days prior to cystectomy and recovered from all associated toxicities at the time of registration. Patients must not have received any prior pelvic irradiation.

Patients must have a Zubrod performance status of 0, 1 or 2 and have adequate hepatic function. All patients must be offered the opportunity to participate in specimen banking for future use.

Stratification/Descriptive Factors

Treatment randomization will be stratified according to the following factors: (1) neoadjuvant chemo-therapy: cisplatin based vs carboplatin based vs other vs none; (2) clinical stage: T2 vs T3 or T4a; and (3) Zubrod performance status: 0-1 vs 2.

Accrual Goals

The accrual goal for this study is 564 eligible randomized patients (282 per arm). At the onset, accrual will be limited to vanguard sites and a feasibility assessment will be conducted after the first 15 patients have been randomized. A second feasibility assessment will be conducted one year after all vanguard sites have IRB approval. If the study continues past the two feasibility assessments, the study will open for registration across all participating sites, with interim analyses planned at 25%, 50%, and 75% information time.

Summary Statement

As of December 31, 2014, 421 patients had been registered to this study, of whom 396 were randomized. The most common reason among the 25 patients not randomized was extent of disease at the time of surgery.

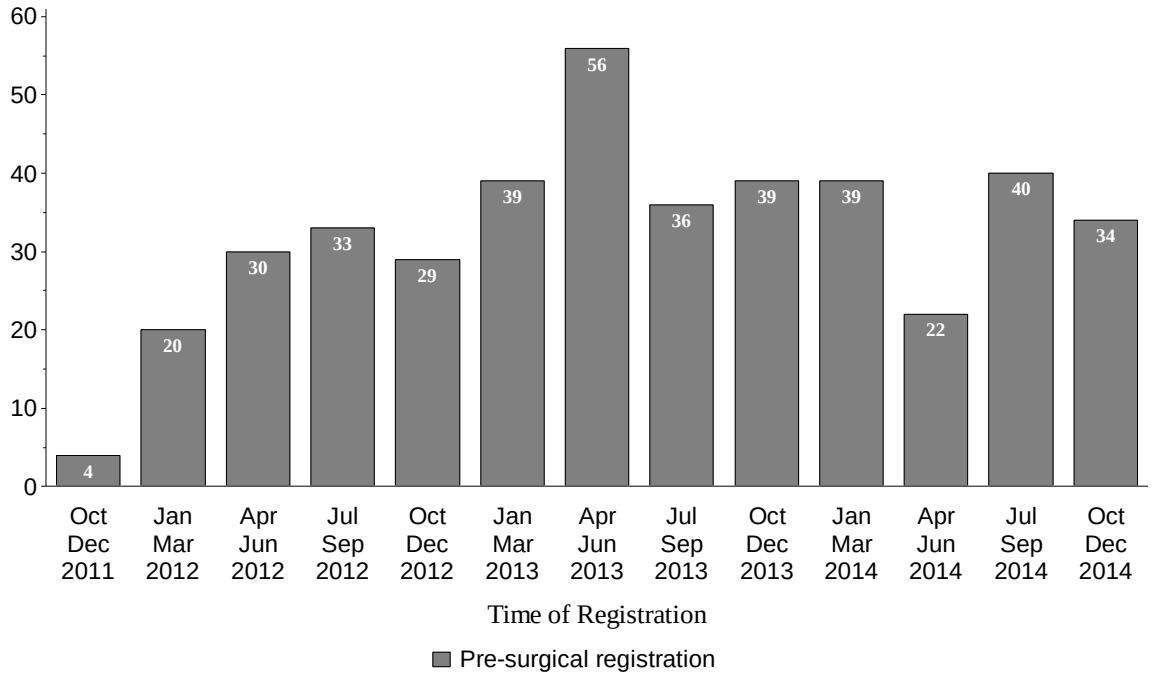
Two hundred patients have been randomized to standard lymph node dissection (LND) and 196 patients randomized to extended LND. Forty-five randomized patients are currently ineligible, including five patients randomized in error and 29 patients with insufficient baseline documentation, 17 of whom are potentially reversible. Major protocol deviations are recorded for two patients who were randomized to the standard LND arm, but received extended LND due to extent of disease at the time of surgery. These two patients are not assessable for adverse events.

Three hundred forty-four patients have been assessed for adverse events. Five patient deaths on the extended LND arm have been reported: one due to a possibly treatment-related thromboembolic event, one due to myocardial infarction along with multi-organ failure, one due to stroke, one due to multiple cardiac comorbidities, and one due to coronary artery disease. This last patient also experienced Grade 4 sepsis and respiratory failure. Eight patients on the extended LND arm experienced Grade 4 adverse events as maximum degree: one with hyperkalemia; one with hyponatremia; one with ileus; one with depression; one with a small intestinal obstruction; one with a thromboembolic event; one with sepsis and leukocytosis; and one with sepsis and right groin exploration, laparotomy, and cecectomy listed as "Surg/medical procedures-Oth" in the table.

Two patient deaths have been reported on the standard LND arm, one due to a thromboembolic event and one due to sepsis. This last patient also experienced Grade 4 DIC and enterovesical fistula. Two patients on the standard LND arm experienced Grade 4 adverse events as maximum degree: one with sepsis; and one with acute kidney injury, sepsis, and thromboembolic event. Twenty-seven patients on the extended LND arm and 18 patients on the

standard LND arm experienced Grade 3 adverse events as maximum degree. Two patients, one on each arm, who did not return for their 90 day assessments are coded as "Other - not protocol specified" for the reason they are off treatment.

Initial Registrations By 3 Month Intervals



Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Alliance	92	Davis, U of CA	11
So Calif, U of	87	Loyola University	10
ECOG-ACRIN	57	NCIC-CTG	9
MD Anderson	41	Cleveland Clinic OH	7
Baylor College	36	San Antonio, TX-UCOP/San Antonio, U of TX	5
San Antonio, U of TX	29	LSU-Shreveport/Gulf South MU-NCORP	4
Oregon Hlth Sci Univ	19	Rochester, Univ of	1
BC Cancer Agency	13	**Total (15 Institutions)**	**421**

Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending December 31, 2014; Data as of March 17, 2015

	Total
NUMBER REGISTERED	421
INELIGIBLE	36
Insufficient Documentation	29
Irreversible	13
Reversible	16
ELIGIBLE	385

Registration, Eligibility, and Evaluability

Randomization

Registrations ending December 31, 2014; Data as of March 17, 2015

	TOTAL	Standard LND	Extended LND
NUMBER REGISTERED	396	200	196
INELIGIBLE	45	26	19
Insufficient Documentation	29	16	13
Irreversible	12	6	6
Reversible	17	10	7
ELIGIBLE	351	174	177
ADVERSE EVENT ASSESSMENT			
Evaluable	344	171	173
Too Early	7	3	4

Patient Characteristics

Randomization

Registrations ending December 31, 2014; Data as of March 17, 2015

	Standard LND (n=174)		Extended LND (n=177)	
AGE				
Median	68.5		68.7	
Minimum	38.6		46.0	
Maximum	90.0		90.4	
SEX				
Males	131	75%	143	81%
Females	43	25%	34	19%
HISPANIC				
Yes	4	2%	11	6%
No	166	95%	157	89%
Unknown	4	2%	9	5%
RACE				
White	156	90%	156	88%
Black	7	4%	9	5%
Asian	5	3%	2	1%
Pacific Islander	0	0%	1	1%
Multi-Racial	2	1%	1	1%
Unknown	4	2%	8	5%

	Standard LND (n=174)		Extended LND (n=177)	
NEOADJUVANT CHEMOTHERAPY				
Cisplatin based	80	46%	83	47%
Carboplatin based	7	4%	8	5%
Other	7	4%	4	2%
None	80	46%	82	46%
CLINICAL STAGE				
T2	127	73%	129	73%
T3 or T4a	47	27%	48	27%
ZUBROD PERFORMANCE STATUS				
0-1	171	98%	175	99%
2	3	2%	2	1%

Treatment Summary

Randomization

Registrations ending December 31, 2014; Data as of March 17, 2015

	TOTAL	Standard LND	Extended LND
NUMBER ON PROTOCOL TREATMENT	13	7	6
NUMBER OFF PROTOCOL TREATMENT	338	167	171
REASON OFF TREATMENT			
Treatment completed as planned	317	157	160
Adverse Event or side effects	0	0	0
Refusal unrelated to adverse event	1	1	0
Other - not protocol specified	2	1	1
Reason under review	1	0	1
MAJOR PROTOCOL DEVIATIONS	2	2	0

Number of Patients with a Given Type and Grade of Adverse Event

Randomization

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2014; Data as of March 17, 2015

	Standard LND (n=171) Grade						Extended LND (n=173) Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
AST increased	171	0	0	0	0	0	172	1	0	0	0	0
Abdominal distension	170	0	1	0	0	0	173	0	0	0	0	0
Abdominal pain	168	2	1	0	0	0	169	2	2	0	0	0
Acidosis	168	1	0	2	0	0	172	0	0	1	0	0
Acute kidney injury	170	0	0	0	1	0	169	1	3	0	0	0
Agitation	171	0	0	0	0	0	171	0	1	1	0	0
Anemia	157	5	4	5	0	0	154	3	9	7	0	0
Anorexia	171	0	0	0	0	0	170	1	1	1	0	0
Atelectasis	171	0	0	0	0	0	171	0	2	0	0	0
Atrial fibrillation	168	1	1	1	0	0	171	0	2	0	0	0
Atrial flutter	171	0	0	0	0	0	172	1	0	0	0	0
Back pain	171	0	0	0	0	0	172	0	1	0	0	0
Bloating	171	0	0	0	0	0	172	1	0	0	0	0

	Standard LND (n=171)						Extended LND (n=173)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Blood/lymph disorder-Other	170	1	0	0	0	0	173	0	0	0	0	0
Cardiac disorder-Other, spec	171	0	0	0	0	0	172	1	0	0	0	0
Cardiac troponin I increased	171	0	0	0	0	0	172	0	0	1	0	0
Catheter related infection	170	0	1	0	0	0	172	0	1	0	0	0
Chills	171	0	0	0	0	0	172	1	0	0	0	0
Colitis	170	0	0	1	0	0	172	0	1	0	0	0
Colonic obstruction	170	1	0	0	0	0	172	0	0	1	0	0
Confusion	171	0	0	0	0	0	172	0	0	1	0	0
Constipation	170	1	0	0	0	0	167	5	0	1	0	0
Cough	171	0	0	0	0	0	172	1	0	0	0	0
Creatinine increased	169	1	1	0	0	0	171	1	1	0	0	0
DIC	170	0	0	0	1	0	173	0	0	0	0	0
Death NOS	171	0	0	0	0	0	171	0	0	0	0	2
Dehydration	171	0	0	0	0	0	171	0	1	1	0	0
Delirium	171	0	0	0	0	0	171	0	0	2	0	0
Depression	171	0	0	0	0	0	171	0	1	0	1	0
Diarrhea	170	1	0	0	0	0	171	1	0	1	0	0
Dysgeusia	171	0	0	0	0	0	172	0	1	0	0	0
Dyspepsia	171	0	0	0	0	0	172	1	0	0	0	0
Dyspnea	171	0	0	0	0	0	171	2	0	0	0	0
Edema limbs	168	2	1	0	0	0	171	1	0	1	0	0
Enterovesical fistula	170	0	0	0	1	0	173	0	0	0	0	0
Erectile dysfunction	170	0	1	0	0	0	173	0	0	0	0	0
Erythema multiforme	171	0	0	0	0	0	172	1	0	0	0	0
Fatigue	170	1	0	0	0	0	170	2	1	0	0	0
Fever	170	1	0	0	0	0	169	2	1	1	0	0
Flank pain	171	0	0	0	0	0	172	1	0	0	0	0
GI disorders-Other, specify	171	0	0	0	0	0	172	0	0	1	0	0
Gastritis	170	0	1	0	0	0	173	0	0	0	0	0
Gastrointestinal fistula	170	0	0	1	0	0	173	0	0	0	0	0
Gen disorders/admin site cond	171	0	0	0	0	0	172	1	0	0	0	0
Generalized muscle weakness	171	0	0	0	0	0	172	0	1	0	0	0
Genital edema	171	0	0	0	0	0	171	2	0	0	0	0
Hematuria	169	1	1	0	0	0	172	1	0	0	0	0
Hypercalcemia	170	0	0	1	0	0	173	0	0	0	0	0
Hyperglycemia	169	1	1	0	0	0	172	0	0	1	0	0
Hyperkalemia	171	0	0	0	0	0	170	0	1	1	1	0
Hypernatremia	171	0	0	0	0	0	172	1	0	0	0	0
Hypertension	170	0	0	1	0	0	172	0	0	1	0	0
Hypoalbuminemia	167	0	3	1	0	0	172	0	1	0	0	0
Hypocalcemia	170	0	1	0	0	0	171	0	2	0	0	0
Hypokalemia	168	1	1	1	0	0	171	1	1	0	0	0
Hyponatremia	170	0	0	1	0	0	168	4	0	0	1	0
Hypophosphatemia	170	0	1	0	0	0	173	0	0	0	0	0
Hypotension	170	0	0	1	0	0	170	1	2	0	0	0
Hypoxia	171	0	0	0	0	0	171	0	1	1	0	0
INR increased	170	1	0	0	0	0	173	0	0	0	0	0
Ileal obstruction	170	0	1	0	0	0	173	0	0	0	0	0
Ileus	163	0	8	0	0	0	154	0	14	4	1	0
Infections/infestations-Other	171	0	0	0	0	0	170	0	1	2	0	0
Inj/poisoning/proced comp-Oth	171	0	0	0	0	0	172	0	0	1	0	0
Intra-abdominal hemorrhage	170	0	0	1	0	0	173	0	0	0	0	0
Intraoperative arterial injury	170	1	0	0	0	0	173	0	0	0	0	0
Intraoperative venous injury	167	2	1	1	0	0	173	0	0	0	0	0
Kidney infection	171	0	0	0	0	0	171	0	0	2	0	0
Leukocytosis	171	0	0	0	0	0	172	0	0	0	1	0
Localized edema	171	0	0	0	0	0	172	1	0	0	0	0
Lung infection	170	0	0	1	0	0	172	0	0	1	0	0
Lymphedema	171	0	0	0	0	0	172	1	0	0	0	0

	Standard LND (n=171)						Extended LND (n=173)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Lymphocele	166	2	2	1	0	0	167	2	2	2	0	0
Lymphocyte count decreased	169	0	2	0	0	0	172	0	0	1	0	0
Multi-organ failure	171	0	0	0	0	0	172	0	0	0	0	1
Myocardial infarction	169	0	0	2	0	0	172	0	0	0	0	1
Nausea	170	0	0	1	0	0	170	2	1	0	0	0
Neoplasms, all	170	0	1	0	0	0	173	0	0	0	0	0
Pain	170	0	1	0	0	0	166	3	4	0	0	0
Pain in extremity	170	0	1	0	0	0	173	0	0	0	0	0
Paresthesia	170	1	0	0	0	0	173	0	0	0	0	0
Pelvic infection	171	0	0	0	0	0	172	0	0	1	0	0
Peripheral motor neuropathy	170	1	0	0	0	0	172	0	1	0	0	0
Peripheral sensory neuropathy	171	0	0	0	0	0	172	0	1	0	0	0
Platelet count decreased	170	1	0	0	0	0	173	0	0	0	0	0
Pulmonary edema	171	0	0	0	0	0	172	0	1	0	0	0
Renal/urinary disorders-Other	170	1	0	0	0	0	173	0	0	0	0	0
Resp/thoracic/mediastinal ds	171	0	0	0	0	0	172	0	1	0	0	0
Respiratory failure	171	0	0	0	0	0	172	0	0	0	1	0
Sepsis	168	0	0	0	2	1	170	0	0	0	3	0
Sinus tachycardia	171	0	0	0	0	0	170	1	1	1	0	0
Small intestinal obstruction	171	0	0	0	0	0	171	0	0	1	1	0
Soft tissue infection	171	0	0	0	0	0	172	0	0	1	0	0
Stroke	171	0	0	0	0	0	172	0	0	0	0	1
Supraventricular tachycardia	171	0	0	0	0	0	172	0	0	1	0	0
Surg/medical procedures-Oth	167	2	0	2	0	0	170	1	1	0	1	0
Thromboembolic event	165	0	4	0	1	1	158	1	6	6	1	1
Ureteric anastomotic leak	171	0	0	0	0	0	172	0	0	1	0	0
Urinary incontinence	167	1	3	0	0	0	172	1	0	0	0	0
Urinary retention	170	0	1	0	0	0	173	0	0	0	0	0
Urinary tract infection	166	0	3	2	0	0	167	0	4	2	0	0
Urinary tract obstruction	171	0	0	0	0	0	171	0	1	1	0	0
Vasc disorders-Other, spec	170	1	0	0	0	0	173	0	0	0	0	0
Venous injury	170	0	0	1	0	0	172	0	1	0	0	0
Vomiting	169	0	1	1	0	0	169	3	1	0	0	0
Weight loss	170	1	0	0	0	0	172	0	1	0	0	0
Wound complication	168	2	1	0	0	0	172	1	0	0	0	0
Wound dehiscence	170	0	1	0	0	0	172	1	0	0	0	0
Wound infection	168	0	2	1	0	0	170	0	2	1	0	0
MAX. GRADE ANY ADVERSE EVENT	115	13	21	18	2	2	99	6	28	27	8	5

S1014 Phase II

Abiraterone Acetate Treatment for Prostate Cancer Patients with a PSA of More Than Four Following Initial Androgen Deprivation Therapy

Study Chairs:
T Flaig, M Hussain

Statisticians:
C Tangen, M Plets

Data Coordinator:
J Barce

Date Activated:
08/09/2011

Date Closed:
08/01/2013

Objectives

To assess the rate of achieving a PSA of ≤ 0.2 ng/ml with abiraterone acetate therapy in patients with metastatic prostate cancer with a suboptimal response to androgen deprivation therapy (ADT).

To assess the overall survival and objective progression-free survival in this population.

To assess PSA partial response in this population.

To evaluate the qualitative and quantitative toxicity in this population treated with abiraterone acetate.

Patient Population

Patients must have a histologically or cytologically proven diagnosis of adenocarcinoma of the prostate. Patients must have had metastatic (M1) disease at the time of initiation of ADT, as evidenced by at least one of the following: visceral disease, bone metastases in either the axial and/or the appendicular skeleton, or distant lymph node disease. Patients must have a suboptimal response to initial ADT induction, with a PSA of > 4 ng/ml between 6-12 months from starting ADT. If the PSA is declining or stable (defined as a PSA rise = 0.1 ng/ml from nadir) and the patient is on an antiandrogen, he must remain on the antiandrogen. Patients with stable or declining PSA who have had previous antiandrogen exposure, but are not taking an antiandrogen at the time of registration, must wait at least 6 weeks from the last antiandrogen dose before registration and still demonstrate a stable or falling PSA which is > 4 ng/ml by month 12, in order to be eligible. If the PSA is rising and patient is on an antiandrogen, formal antiandrogen washout must be performed. Patients with a history of brain metastases or who currently have treated or untreated brain metastases are not eligible.

Patients must be receiving ADT (e.g., LHRH agonist with or without antiandrogen) prior to entering the study. Patients with a history of prior neoadjuvant or adjuvant GNRH agonist therapy (related to previous surgery or radiation) are eligible provided they finished therapy at least two years prior to registration. Finasteride and dutasteride therapies are allowed provided they have been stopped at least six weeks prior to registration. Patients must not have received any prior cytotoxic chemotherapy or radiopharmaceuticals for prostate cancer. Previous ketoconazole therapy for the treatment of prostate cancer is not allowed. Patients requiring more than 10 mg a day of prednisone for another medical indication are not eligible. Patients must not have received any prior Provenge. At least 28 days must have elapsed since completion of prior radiation therapy or surgery.

Patients must have a Zubrod performance status of 0-2 and a testosterone value < 50 ng/dl. Patients must have controlled blood pressure defined as systolic blood pressure < 160 mmHg and/or diastolic blood pressure < 95 mmHg. Patients must not have a history of pituitary or adrenal dysfunction, active or symptomatic viral hepatitis or chronic liver disease, or a history of New York Heart Association Class III and IV heart failure.

Accrual Goals
The accrual goal for this study is 38 eligible patients.

Summary Statement
This study was permanently closed on August 1, 2013, after reaching its accrual goal with 41 patients registered. All patients are eligible. One patient who did not receive any protocol treatment due to worsening bone pain and metastatic disease is not analyzable for any endpoint.

Forty patients have been assessed for adverse events. Two patients experienced Grade 4 adverse events, one with increased ALT, and one with rectal hemorrhage. Twelve additional patients experienced Grade 3 toxicities as maximum degree: one with lung infection; one with anorexia; one with weight gain; one with nausea, vomiting and hypokalemia; two with hypertension; one with nausea and vomiting; one with hypertension and thromboembolic event; one with hyperglycemia; one with hyperglycemia and leukocytosis; one with hypokalemia; and one with increased INR, ALT and AST. Eleven patients are still receiving protocol treatment.

The primary endpoint of this study was undetectable PSA response (≤ 0.2 ng/ml). If the proportion of men with undetectable PSA is ≥ 20%, the regimen would be of further interest, whereas further testing would not be pursued if the proportion of men with undetectable PSA is ≤ 5%. Patients were evaluated for PSA response within 12 months of starting abiraterone acetate therapy. Five (13%) patients achieved an undetectable PSA of ≤ 0.2ng/ml (95% CI: 4%, 27%). Nine (23%) additional patients had PSA level > 0.2 but < 4 ng/ml (95% CI: 11%, 38%). Twenty-six patients had no PSA response and are assumed to be non-responders. Although five patients attaining undetectable (≤ 0.2 ng/ml) PSA responses to abiraterone acetate therapy in this poor prognosis setting is an encouraging result, this study did not reach the protocol pre-specified level of six responses out of 40. The median progression-free survival was 17 months (95% CI: 9, 20) and the median overall survival was 24 months.

Registration by Institution

Institutions	Total Reg	Institutions	Total Reg
Utah, U of	7	Henry Ford Hosp	1
Baylor College	5	Kansas, U of	1
Colorado, U of	3	LSU-Shreveport/Gulf South MU-NCORP	1
Wayne State Univ	3	Mem Hosp, Co Springs/Colorado, U of	1
Yale University	3	Montana NCORP	1
City of Hope Med Ctr	2	Southeast CCC NCORP	1
Kaiser NCORP	2	SW Cancer & Res Ctr/San Antonio, U of TX	1
Nevada CRF NCORP	2	Tulane Univ MBCCOP	1
So Calif, U of	2	UF Cancer Center/Arkansas, U of	1
Wichita NCORP	2	**Total (20 Institutions)**	**41**
Hawaii MU-NCORP	1		

Registration, Eligibility, and Evaluability

Data as of February 3, 2015

	Abiraterone Acetate
NUMBER REGISTERED	41
ELIGIBLE	41
Not Analyzable	1
ADVERSE EVENT ASSESSMENT	
Evaluable	40

Patient Characteristics

Data as of February 3, 2015

	Abiraterone Acetate (n=40)	
AGE		
Median	66.3	
Minimum	39.1	
Maximum	85.1	
HISPANIC		
Yes	4	10%
No	34	85%
Unknown	2	5%
RACE		
White	27	67%
Black	10	25%
Asian	2	5%
Native American	1	2%

Treatment Summary

Data as of February 3, 2015

	Abiraterone Acetate
NUMBER ON PROTOCOL TREATMENT	11
NUMBER OFF PROTOCOL TREATMENT	29
REASON OFF TREATMENT	
Adverse Event or side effects	5
Refusal unrelated to adverse event	1
Progression/relapse	16
Death	0
Other - not protocol specified	7
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

Number of Patients with a Given Type and Grade of Adverse Event

Adverse Events Unlikely or Not Related to Treatment Excluded

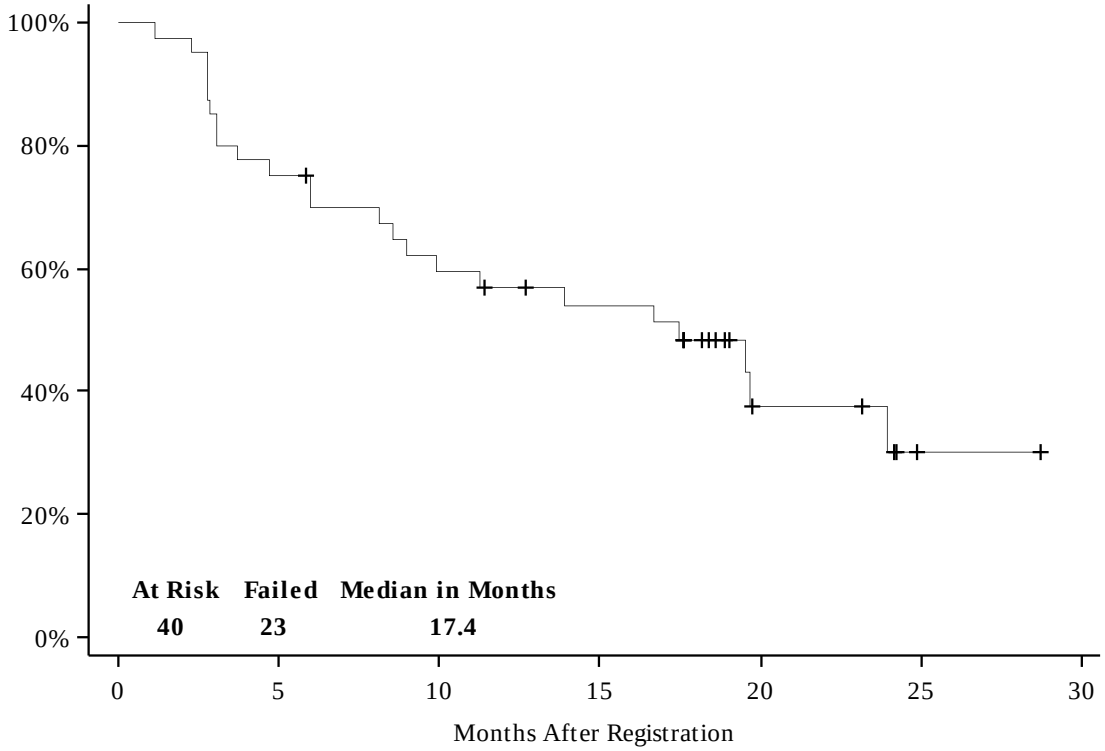
Data as of February 3, 2015

ADVERSE EVENT	Abiraterone Acetate (n=40) Grade 0	1	2	3	4	5
ALT increased	32	4	2	1	1	0
AST increased	31	7	0	2	0	0
Abdominal pain	38	1	1	0	0	0
Alkaline phosphatase increased	30	10	0	0	0	0
Anemia	32	7	1	0	0	0
Anorexia	38	1	0	1	0	0
Arthralgia	39	1	0	0	0	0
Blood bilirubin increased	37	2	1	0	0	0
Blood/lymph disorder-Other	37	2	1	0	0	0
Bruising	37	3	0	0	0	0
Chest pain - cardiac	39	1	0	0	0	0
Cholesterol high	39	1	0	0	0	0
Constipation	39	1	0	0	0	0
Cough	39	1	0	0	0	0
Creatinine increased	37	3	0	0	0	0
Cushingoid	39	1	0	0	0	0
Dizziness	39	1	0	0	0	0
Dry eye	39	1	0	0	0	0
Dysgeusia	39	1	0	0	0	0
Dyspepsia	39	0	1	0	0	0
Dyspnea	39	0	1	0	0	0
Edema limbs	34	6	0	0	0	0
Edema trunk	39	1	0	0	0	0
Fatigue	27	9	4	0	0	0
Flank pain	39	1	0	0	0	0
GERD	39	1	0	0	0	0
Headache	38	0	2	0	0	0
Hot flashes	31	6	3	0	0	0
Hypercalcemia	39	1	0	0	0	0
Hyperglycemia	30	8	0	2	0	0
Hypernatremia	37	3	0	0	0	0

ADVERSE EVENT	Abiraterone Acetate (n=40) Grade 0	1	2	3	4	5
Hypertension	29	2	6	3	0	0
Hypoalbuminemia	38	2	0	0	0	0
Hypokalemia	37	1	0	2	0	0
Hyponatremia	39	1	0	0	0	0
Hypophosphatemia	39	0	1	0	0	0
INR increased	39	0	0	1	0	0
Insomnia	37	2	1	0	0	0
Leukocytosis	39	0	0	1	0	0
Lung infection	38	0	1	1	0	0
Lymphocyte count decreased	39	1	0	0	0	0
MS/connective tissue disorder	39	1	0	0	0	0
Myalgia	37	3	0	0	0	0
Nail ridging	39	1	0	0	0	0
Nausea	35	3	0	2	0	0
Pain	39	1	0	0	0	0
Pain in extremity	39	1	0	0	0	0
Pelvic pain	39	1	0	0	0	0
Personality change	39	0	1	0	0	0
Platelet count decreased	39	1	0	0	0	0
Pruritus	39	1	0	0	0	0
Rash acneiform	38	2	0	0	0	0
Rectal hemorrhage	39	0	0	0	1	0
Skin/subq tissue ds-Other	39	1	0	0	0	0
Spasticity	39	1	0	0	0	0
Thromboembolic event	39	0	0	1	0	0
Upper respiratory infection	39	0	1	0	0	0
Vomiting	38	0	0	2	0	0
Weight gain	37	2	0	1	0	0
Weight loss	39	0	1	0	0	0
White blood cell decreased	39	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	4	9	13	12	2	0

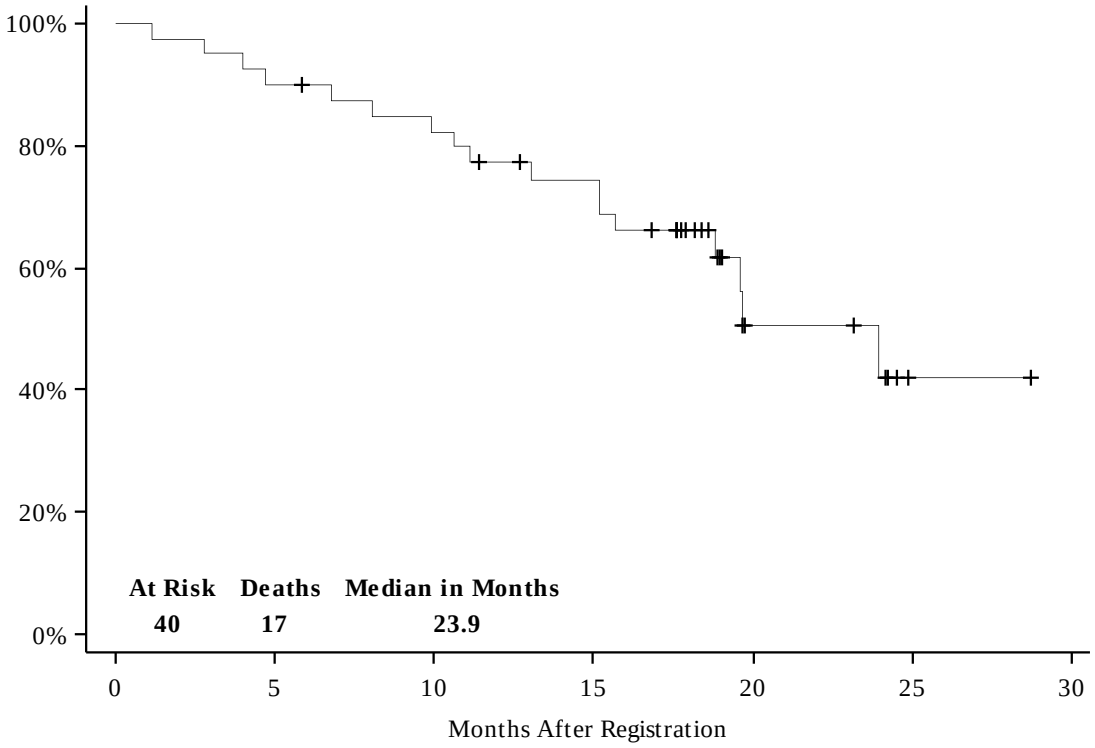
Progression-Free Survival

Data as of February 3, 2015



Overall Survival

Data as of February 3, 2015



S1204 Surveillance

A Sero-Epidemiologic Survey and Cost-Effectiveness Study of Screening for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Among Newly Diagnosed Cancer Patients

Study Chairs:
S Ramsey, R Loomba, R Chugh, D Hershman, J Hwang

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Date Activated:
08/29/2013

Date Closed:
12/15/2014*

*Temporary closure

Objectives

Among newly diagnosed cancer patients presenting to SWOG-affiliated community and academic oncology clinics, estimate the prevalence of human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) infection.

Evaluate known sociodemographic, clinical, and behavioral factors that are significantly associated with previously undiagnosed HIV, HBV, and/or HCV infection in a population of people with newly diagnosed cancer.

Among patients who are identified as having HIV, HBV, and/or HCV, evaluate the timing and type of treatments received, both for the viral infections and the cancers.

Evaluate type and rate of cancer treatment-related adverse events in patients with HIV, HBV, and/or HCV infection.

Determine the cost-effectiveness of (1) routine, universal screening and (2) risk factor-directed screening of newly diagnosed cancer patients for HIV, HBV and/or HCV versus current care.

Create a biorepository of stored serum for future translational medicine studies that may include identifying genomic and viral factors that increase the risk of serious adverse effects among participants infected with HIV, HBV, and/or HCV being treated for invasive cancers.

Patient Population

Patients must be presenting for evaluation or treatment for the first diagnosis of a new cancer malignancy (including hematologic). Confirmed pathologic diagnosis must be within 120 days of registration. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Individuals are ineligible if they have been diagnosed with a malignancy other than the current malignancy within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer. Individuals are eligible if they have had no evidence of disease for a prior malignancy, except as noted above, for at least five years prior to randomization.

Patients must be 18 years of age or older. Patients must have had their blood drawn for testing for HIV, HBV and HCV prior to registration. Patients who have had HIV, HBV and/or HCV testing within 60 days prior to registration and who do not wish to be retested are eligible, provided supporting documents can be obtained confirming viral test results for all three viruses. Patients who are viral positive for either HIV, HBV, and/or HCV and who do not wish

to be retested are eligible, provided documentation of viral load within 120 days prior to registration can be obtained. Note that these patients must be tested for or provide current viral load for all three viruses to be eligible. All documentation must be obtained prior to registration. Patients are allowed to participate in other clinical trials.

Cancer Control Credits
No cancer control credits are awarded for this study.

Accrual Goals
A total of 3,000 eligible patients will be accrued.

Summary Statement
For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1216 Phase III

Coordinating Group: SWOG

A Phase III Randomized Trial Comparing Androgen Deprivation Therapy + TAK-700 with Androgen Deprivation Therapy + Bicalutamide in Patients with Newly Diagnosed Metastatic Hormone Sensitive Prostate Cancer

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Participants:
SWOG, CTSU (supported by Alliance, ECOG-ACRIN)

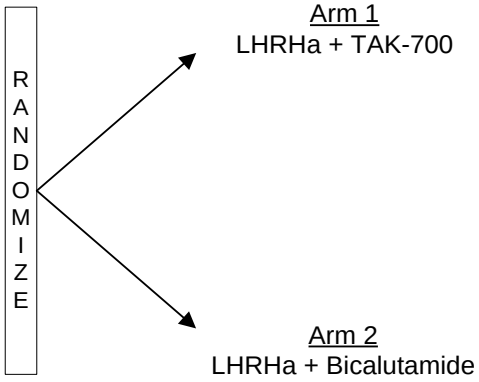
Date Activated:
03/01/2013

Study Chairs:
N Agarwal, D Vaena, G MacVicar

Statisticians:
C Tangen, M Plets

Data Coordinator:
A Hamm

SCHEMA



Objectives

To compare overall survival in newly diagnosed metastatic prostate cancer patients randomly assigned to androgen deprivation therapy (ADT) + TAK-700 versus ADT + bicalutamide.

To compare progression free survival between ADT + TAK-700 versus ADT + bicalutamide.

To compare distributions of PSA response (< 0.2 vs 0.2-4.0 vs > 4.0 ng/ml) between the treatment arms at 7 months post-randomization.

To compare the qualitative and quantitative adverse events from each treatment arm.

To characterize the long-term survival in both treatment arms after 10 years of follow-up.

To validate the prognostic and predictive value of markers of bone turnover in newly diagnosed metastatic hormone sensitive prostate cancer patients treated with TAK-700.

To evaluate genomic variants and gene expression of androgen pathway genes and their correlation with response to therapy.

To bank serum/whole blood and tissue specimens for future use.

To evaluate genomic variants and gene expression of androgen pathway genes and their correlation with response to therapy (ADT + TAK-700 vs ADT + bicalutamide).

Patient Population

Patients must have a histologically or cytologically proven diagnosis of adenocarcinoma of the prostate. All patients must have metastatic disease as evidenced by soft tissue and/or bony metastases prior to initiation of androgen deprivation therapy. Patients must have a PSA = 2 ng/mL obtained within 90 days prior to registration. Patients with known brain metastases are not eligible.

Patients who have not started any therapy with LHRH agonist or antagonist (or orchiectomy) (Early Induction Group) and patients who have already started therapy with LHRH agonist or antagonist (or orchiectomy) within the 30 days prior to registration (Late Induction Group) are eligible. Patients must be registered within 30 days of first injection of the LHRH agonist or antagonist (or orchiectomy). In the late induction group, if the method of castration was LHRH agonists, the patient must be willing to continue the use of LHRH agonist and add bicalutamide or TAK-700 (according to randomization) during protocol treatment; if the patient was on an antiandrogen, the patient must be willing to switch over to bicalutamide or TAK-700 (according to randomization), no washout is required; if the method of castration was LHRH antagonists, the patient must be willing to switch to an LHRH agonist during protocol treatment. Patients must not have received prior and/or have any plans for receiving concomitant therapy with ketoconazole, aminoglutethimide, abiraterone acetate, or enzalutamide (MDV3100). Patients must not have received any prior cytotoxic chemotherapy for metastatic prostate cancer. At least six months must have elapsed since completion of prior neoadjuvant and/or adjuvant androgen deprivation therapy. Concomitant radiotherapy is allowed only for baseline symptoms per investigator's clinical judgment during the first four months of protocol treatment.

Patients must have adequate hematologic, hepatic, renal, and cardiac function, and have a Zubrod performance status of 0-2 (or 3 if from bone pain only). Patients must have a DEXA scan obtained within two years prior to registration. Patients must not have Class III or IV heart failure at the time of screening, uncontrolled hypertension, known HIV infection, or active chronic hepatitis B or C. Patients with a known history of primary and secondary adrenal insufficiency are not eligible. Patients must not be known to have hypersensitivity to TAK-700, TAK-700 metabolites, bicalutamide, or LHRH agonist. All patients must be offered the opportunity to participate in specimen banking for future use.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) severity of disease: extensive vs minimal; (2) Zubrod performance status: 0-1 vs 2-3 (if performance status is 3, it is due to bone pain only); and (3) pre-registration treatment status: early induction vs late induction.

Accrual Goals

The accrual goal for this study is 1,486 eligible patients (743 eligible patients per arm). Five interim analyses will be performed when there is 24%, 45%, 62%, 77%, and 89% information.

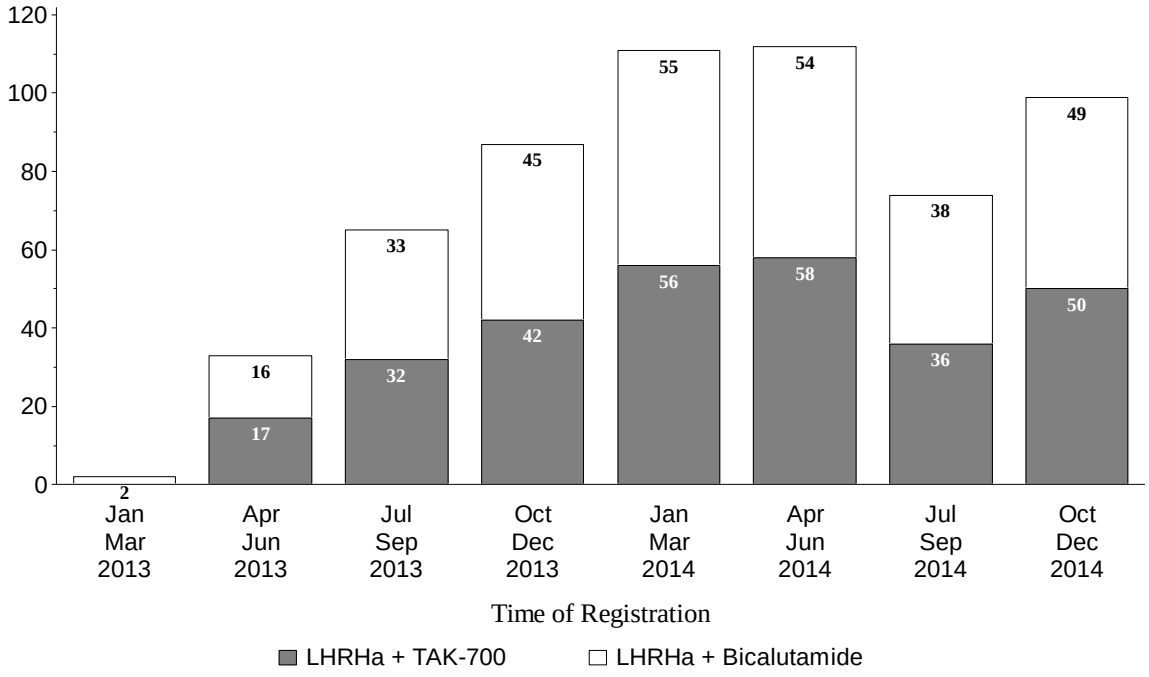
Summary Statement

As of December 31, 2014, 583 patients had been registered to this study. Two hundred ninety-one patients were randomized to the LHRHa + TAK-700 arm and 292 patients were randomized to the LHRHa + bicalutamide arm. Fifty-four patients are currently ineligible. Thirty-seven are due to insufficient baseline documentation, 27 of whom are potentially reversible. A major deviation is coded for one patient on the LHRHa + bicalutamide arm who did not receive any protocol treatment after registration due to death prior to protocol treatment; This patient is not assessable for adverse events. One other patient on the LHRHa + bicalutamide arm is not evaluable for adverse events or progression due to patient refusal after seven days of treatment and no further follow-up.

Four hundred ninety-five patients have been assessed for adverse events. No Grade 4 or 5 toxicities were reported on the standard arm. One patient death due to myocardial infarction was reported on the LHRHa

+ TAK-700 arm. Six patients on this arm experienced Grade 4 adverse events: increased ALT, encephalopathy, ventricular fibrillation, increased lipase, increased serum amylase, increased blood bilirubin and hypokalemia. An additional 66 patients on the LHRHa + TAK-700 arm and 15 patients on the LHRHa + bicalutamide arm experienced Grade 3 toxicities as maximum degree.

Initial Registrations By 3 Month Intervals



Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Alliance	128	Loma Linda Univ	4
ECOG-ACRIN	116	Oregon Hlth Sci Univ	4
Utah, U of	55	Boston MC MBCCOP	3
City of Hope Med Ctr	27	Carolinas Med Ctr/San Antonio, U of TX	3
Nevada CRF NCORP	25	Colorado, U of	3
H Lee Moffitt CC	20	Columbus NCORP	3
Heartland NCORP	16	San Diego, U of CA	3
Michigan, U of	16	Wichita NCORP	3
Kansas, U of	15	Arkansas, U of	2
Kaiser NCORP	14	Fred Hutchinson CRC	2
So Calif, U of	14	Good Samaritan Hosp/Oregon Hlth Sci Univ	2
Davis, U of CA	10	Loyola University	2
Michigan CRC NCORP	8	Montana NCORP	2
Kentucky, U of	7	Ozarks Reg NCORP	2
New Mexico MU-NCORP	7	Rockwood Clinic, PS/PCRC NCORP	2
NRG	7	Southeast CCC NCORP	2
Yale University	7	St Elizabeth's MC/Davis, U of CA	2
Northwest NCORP	6	St Joseph's/Candler/H Lee Moffitt CC	2
Rochester, Univ of	6	UF Cancer Center/Arkansas, U of	2
Baylor College	5	West Michigan NCORP	2
Arizona MC, U of	4	All Other Institutions	12
Dayton NCORP	4	**Total (55 Institutions)**	**583**
Irvine, U of CA	4		

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2014; Data as of February 5, 2015

	TOTAL	LHRHa + TAK-700	LHRHa + Bicalutamide
NUMBER REGISTERED	583	291	292
INELIGIBLE	54	23	31
Insufficient Documentation	37	15	22
Irreversible	10	2	8
Reversible	27	13	14
ELIGIBLE	529	268	261
Analyzable, Pend. Elig.	39	18	21
ADVERSE EVENT ASSESSMENT			
Evaluable	495	255	240
Not Evaluable	2	0	2
Too Early	32	13	19

Patient Characteristics

Registrations ending December 31, 2014; Data as of February 5, 2015

	LHRHa + TAK-700 (n=268)		LHRHa + Bicalutamide (n=261)	
AGE				
Median	67.0		67.1	
Minimum	47.3		19.4	
Maximum	85.7		92.4	
HISPANIC				
Yes	16	6%	13	5%
No	241	90%	234	90%
Unknown	11	4%	14	5%
RACE				
White	230	86%	227	87%
Black	22	8%	22	8%
Asian	5	2%	5	2%
Native American	1	0%	0	0%
Multi-Racial	3	1%	0	0%
Unknown	7	3%	7	3%

	LHRHa + TAK-700 (n=268)		LHRHa + Bicalutamide (n=261)	
SEVERITY OF DISEASE				
Minimal	115	43%	116	44%
Extensive	153	57%	145	56%
ZUBROD PERFORMANCE STATUS				
0 - 1	259	97%	254	97%
2 - 3	9	3%	7	3%
PRE-REG TREATMENT STATUS				
Early induction	134	50%	124	48%
Late induction	134	50%	137	52%

Treatment Summary

Registrations ending December 31, 2014; Data as of February 5, 2015

	TOTAL	LHRHa + TAK-700	LHRHa + Bicalutamide
NUMBER ON PROTOCOL TREATMENT	377	208	169
NUMBER OFF PROTOCOL TREATMENT	152	60	92
REASON OFF TREATMENT			
Adverse Event or side effects	14	11	3
Refusal unrelated to adverse event	28	9	19
Other - not protocol specified	21	8	13
Reason under review	20	10	10
MAJOR PROTOCOL DEVIATIONS	1	0	1

Number of Patients with a Given Type and Grade of Adverse Event

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2014; Data as of February 5, 2015

	LHRHa + TAK-700 (n=255)						LHRHa + Bicalutamide (n=240)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Cardiovascular	168	13	36	36	1	1	227	9	3	1	0	0
Clotting	254	0	1	0	0	0	240	0	0	0	0	0
Dermatologic	220	27	7	1	0	0	229	9	2	0	0	0
EX	254	1	0	0	0	0	240	0	0	0	0	0
Ear	254	1	0	0	0	0	240	0	0	0	0	0
Endocrine	115	116	23	1	0	0	98	118	23	1	0	0
Eye	254	1	0	0	0	0	240	0	0	0	0	0
Flu-like Symptoms	114	91	37	13	0	0	138	77	21	4	0	0
Gastrointestinal	144	73	25	13	0	0	191	37	11	1	0	0
Hematologic	206	44	5	0	0	0	203	32	4	1	0	0
IV	249	6	0	0	0	0	239	1	0	0	0	0
Immunological	252	2	0	1	0	0	240	0	0	0	0	0
Infection	245	1	5	4	0	0	236	1	3	0	0	0
Liver	249	1	0	5	0	0	240	0	0	0	0	0
Lung	237	14	3	1	0	0	234	5	1	0	0	0
Lymphatics	233	18	4	0	0	0	235	5	0	0	0	0
Metabolic	160	60	19	12	4	0	176	48	10	6	0	0
Musculoskeletal	195	46	13	1	0	0	201	30	8	1	0	0
Neurologic	197	44	10	3	1	0	214	21	4	1	0	0
PS	232	16	3	4	0	0	223	13	3	1	0	0
Pain	237	14	3	1	0	0	230	9	1	0	0	0
Renal/Bladder	239	10	5	1	0	0	229	9	2	0	0	0
Sexual/Reproductive Function	232	12	9	2	0	0	196	31	12	1	0	0
Syndromes	253	2	0	0	0	0	237	3	0	0	0	0
VA	252	1	2	0	0	0	238	1	0	1	0	0
MAX. GRADE ANY ADVERSE EVENT	25	74	83	66	6	1	39	119	67	15	0	0

S1314 Phase II

Coordinating Group: SWOG

A Randomized Phase II Study of Co-Expression Extrapolation (COXEN) with Neoadjuvant Chemotherapy for Localized, Muscle-Invasive Bladder Cancer

---

Participants:
SWOG, CTSU

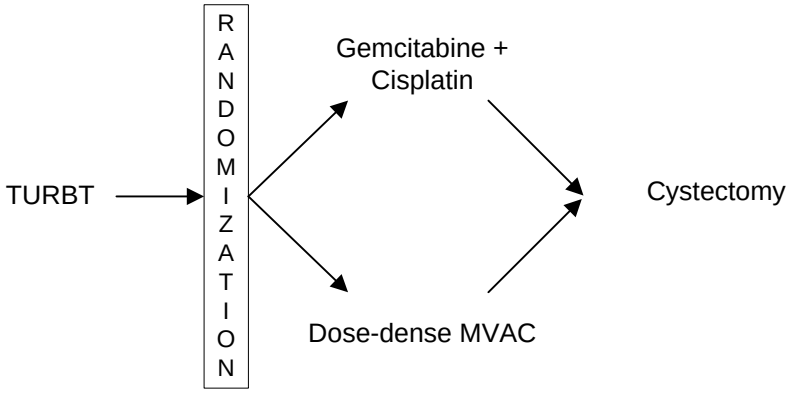
Date Activated:
07/11/2014

Study Chairs:
T Flaig, S Lerner, S Daneshmand

Statisticians:
C Tangen, M Plets

Data Coordinator:
J Barce

SCHEMA



Objectives

To characterize the relationship of DDMVAC- and GC-specific COXEN scores in terms of pT0 rate at cystectomy in patients treated with neoadjuvant chemotherapy.

To assess, in a hypothesis generating fashion, the ability of COXEN to select for an individual chemotherapy regimen (GC vs DDMVAC).

To assess the value of gene expression profiling in predicting overall survival (OS) in bladder cancer patients treated with neoadjuvant chemotherapy.

To assess the difference in pT0 rate between the 21-day GC and 14-day DDMVAC arms, regardless of gene expression.

To assess the safety and tolerability of 21-day GC and 14-day DDMVAC chemotherapy when given in the neoadjuvant setting for bladder cancer.

To assess other translational endpoints via gene expression, tissue microarray, microRNA, SNP and genetic profiling data collected in the neoadjuvant bladder cancer setting.

Patient Population

Patients must have histologically proven stage cT2-T4a N0 M0 urothelial carcinoma of the bladder and documented muscle invasion. Confirmation of diagnosis and staging must be within 56 days prior to registration via imaging, cystoscopy and TURBT. Patients with pure small cell carcinoma, pure adenocarcinoma and pure squamous cell carcinoma are excluded. Patients must have tumor tissue from TURBT that is sufficient for COXEN testing obtained within 56 days prior to registration and must agree to submission of tissue slides. Patients must be planning to receive a cystectomy from a urologist with experience as outlined in protocol.

Patients who have received previous systemic cytotoxic chemotherapy or systemic anthracycline are not eligible.

Patients must have a Zubrod performance status of 0-1 and adequate cardiac, neurologic, hearing, renal, hepatic and hematologic function.

Patients must agree to participate in submission of appropriate specimens and translational medicine studies.

Stratification/Descriptive Factors

Randomization will be stratified according to the following factors: (1) prior systemic therapy: one vs none; (2) performance status: 0 vs 1.

Accrual Goals

The accrual goal for this study is 212 patients to achieve 184 eligible patients.

Summary Statement

As of December 31, 2014, three patients had been registered to this study, two from NRG and one from Nevada CRF NCORP. This study is currently in the process of being amended to make enrollment of patients more feasible. Prominent changes include allowing slides instead of blocks for pathology submission and removing the requirement for minimum number of cystectomies performed by the treating urologist.

S1316 MBO Treatment Study

Coordinating Group: SWOG

Prospective Comparative Effectiveness Trial For Malignant Bowel Obstruction

---

Participants:
SWOG, Alliance

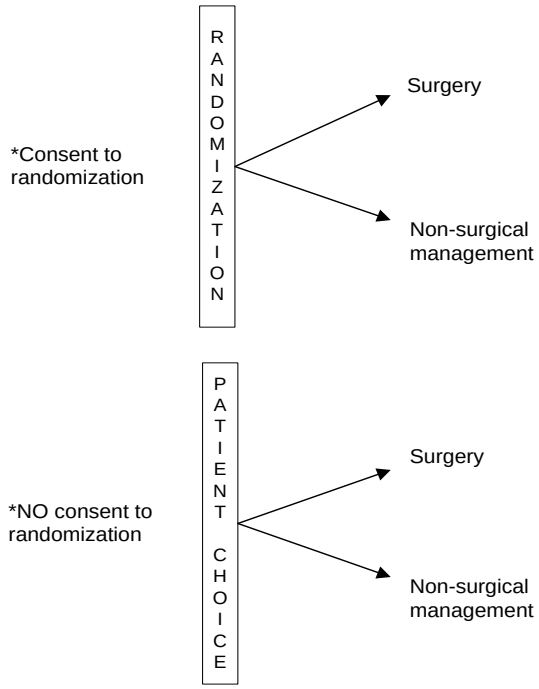
Date Activated:
03/09/2015

Study Chairs:
R Krouse, B Bagwell, A Abernethy

Statisticians:
G Anderson, K Arnold

Data Coordinator:
R Topacio

SCHEMA



*Patients will be enrolled into either the randomized or patient choice portion, not both

Objectives

To compare quality of life, as assessed by the number of days alive and residing outside of the hospital within the first 91 days (13 weeks) after registration, among patients with malignant bowel obstruction (MBO) who receive surgical intervention and similar patients treated non-surgically.

To explore whether there are differences in other health related quality of life (HRQOL) factors of particular interest in this population, including ability to eat, days with nasogastric tube, development of nausea, days of intravenous hydration, days eating solid foods and days drinking that are different for patients with MBO who receive surgical intervention as compared to non-surgical intervention.

To explore whether overall survival is different for patients with MBO who receive surgical intervention as compared to non-surgical intervention. To estimate the effects of surgical versus non-surgical management on quality of life after adjustment for non-adherence to initially assigned/chosen treatment.

To explore whether there are clinical factors (e.g., ascites, albumin, carcinomatosis) that predict better quality of life outcomes for patients with MBO who receive surgical intervention as compared to non-surgical intervention.

Patient Population

Patients must have clinical evidence of a bowel obstruction (via history, physical, and radiographic examination) distal to ligament of Treitz. Patients must have intra-abdominal primary cancer with incurable disease. Patients must not have signs of bowel perforation or "acute" abdomen as evidenced by free air on radiologic imaging or peritonitis on physical exam within two days prior to registration.

Patients must be registered to the study within three days after surgical consult for MBO and prior to any treatment (surgical or non-surgical) for MBO.

Patients must be able to tolerate a major surgical procedure based on clinical evaluation, status of their cancer, and any other underlying medical problems. A member of the patient's surgical team must indicate equipoise for the benefit of the surgical treatment for MBO. Patients must be 18 years or older and have Zubrod performance status of 0-2 within seven days prior to registration. Serum albumin must be planned to be collected after hospital admission, but prior to treatment. Patients must be able to complete the study questionnaires in English.

Stratification/Descriptive Factors

Participant randomization will be stratified by primary tumor type: colorectal cancer vs ovarian cancer vs other cancer.

Cancer Control Credits

The NCI Division of Cancer Prevention has assigned 1.0 cancer control credit (1.6 credits for High Performance sites) per registration to this study.

Accrual Goals

A total of 200 patients will be accrued with a target of at least 50 patients in the randomized component.

Summary Statement

For the current status of this study, please refer to the Cancer Survivorship chapter.

A031201 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

Phase III Trial of Enzalutamide (NSC # 766085) Versus Enzalutamide, Abiraterone, and Prednisone for Castration-Resistant Metastatic Prostate Cancer

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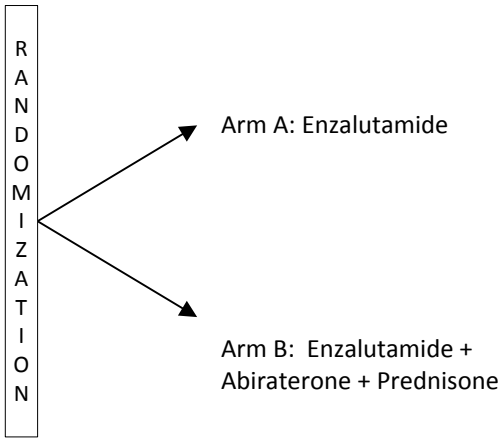
Participants:
Alliance, CTSU

Date Activated:
11/22/2013

Study Chairs:
M Morris (Alliance), A Goldkorn (SWOG)

SCHEMA



Objectives

To compare the overall survival of patients with progressive metastatic CRPC treated with either a) enzalutamide only or b) enzalutamide with abiraterone and prednisone.

To assess the grade 3 or higher toxicity profile and compare safety by treatment arm.

To assess and compare post-treatment PSA declines by treatment arm.

To compare radiographic progression free survival defined by Prostate Cancer Working Group 2 (PCWG2), and objective response rate, by treatment arm.

To test for rPFS treatment interaction in predicting overall survival.

To assess pre- and post-treatment measures of tumor burden and bone activity using NaF PET/CT and Tc MDP bone scintigraphy and correlate these measures with overall survival.

To develop and validate prognostic and predictive models of overall survival that include baseline clinical and molecular markers.

To determine whether pre-treatment serum adrenal androgen (SA) levels are prognostic factors of overall survival and to test whether SA levels are predictive factors of overall survival.

To evaluate specific pre-treatment RNA levels as prognostic factors for OS, including the 6- and 9-gene signatures, the CTC RNA profile, and the circulating tumor stem cell RNA profile.

To evaluate the predictive ability of specific pre-treatment and post-treatment RNA levels on the OS and PFS.

To evaluate specific pre-treatment microRNA levels as prognostic factors for OS.

To test whether the microRNA are predictive factors for overall survival.

To determine whether pre-treatment angiokine levels are prognostic factors for OS and PFS.

To test whether pre-treatment angiokine levels are predictive factors for OS and PFS and to assess whether post-treatment angiokine levels are predictive factors for OS and PFS.

To investigate a drug by CYP17A1 interaction with respect to overall survival.

To assay candidate variants and loci hypothesized to be associated with other clinical phenotypes (e.g., progression-freesurvival or toxicity) or other eQTLs.

To identify specific SNPs and/or copy number variations that are associated with the response to and toxicity associated with therapy.

To define the effect of abiraterone on reducing enzalutamide metabolic clearance (i.e. increasing enzalutamide AUC) when the drugs are used in combination.

To define the exposure (AUC) toxicity and exposure (AUC) anti-tumor effect relationship, including biomarkers for enzalutamide alone and enzalutamide combined with abiraterone in prostate cancer patients.

To develop a population pharmacokinetic model for enzalutamide alone and enzalutamide combined with abiraterone taking account of relevant intrinsic and extrinsic factors.

To determine the intra-patient and inter-patient variability of abiraterone exposure (AUC) in prostate cancer patients receiving abiraterone when combined with enzalutamide.

To determine the intra-patient and inter-patient variability of enzalutamide exposure (AUC) in prostate cancer patients receiving enzalutamide alone and abiraterone plus enzalutamide.

Patient Population

Patients must have progressive CRPC with histologically or cytologically confirmed adenocarcinoma of the prostate. Patients must have measurable or non measurable disease. Patients must have progressive disease at study entry. Patients must not have known or suspected brain metastases (patients with treated epidural disease are eligible).

Patients must not have had prior treatment with taxane-based chemotherapy for metastatic disease. Within four weeks prior to enrollment, patients must not have had treatment with hormonal therapy (including AR antagonists, 5-alpha reductase inhibitors, estrogens) other than GnRH analogues or antagonists, chemotherapy, biologic therapy, investigational therapy, or immunotherapy for prostate cancer. Patients must not have used systemic steroids equivalent to greater than 10mg of prednisone/prednisolone per day. Patients must have had no prior radiation therapy or beta-emitting radionuclide therapy, and have had no major surgery. Patients must not have had prior treatment with enzalutamide, abiraterone, or other novel antiandrogen or androgen synthesis inhibitor. Patients must not have used ketoconazole for greater than seven days. Patients must maintain ongoing androgen deprivation therapy with a GnRH analogue, antagonist, or bilateral orchiectomy. Patients receiving bisphosphonate therapy or denosumab must be on a stable dose for at least four weeks prior to enrollment.

Patients must have adequate hematologic, renal, hepatic, and cardiac function and an ECOG performance status of 0-1. Patients must not have planned palliative procedures for alleviation of bone pain, any structurally unstable bone lesions suggesting impending fracture, history of seizure or any condition that may increase the risk of seizure,

history of TIA within 12 months of enrollment, or GI disorder that negatively affects absorption.

Accrual Goals

A total of 1,224 patients will be accrued to this study (612 per arm). Interim analyses will be performed after 37% information is attained and then every six months until full information.

Summary Statement

Alliance reported a total accrual of 300 patients as of December 31, 2014, including 44 CTSU registrations from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Cleveland Clinic OH	16	Birmingham, U of AL	1
Arizona MC, U of	6	Hawaii MU-NCORP	1
Davis, U of CA	3	Irvine, U of CA	1
Heartland NCORP	3	KaiserPermanenteCOL/Kaiser NCORP	1
Henry Ford Hosp	3	Shaw Reg Cancer Ctr/Colorado, U of	1
VAMC-West Haven/Yale University	3	St Joseph's/Candler/H Lee Moffitt CC	1
Harrison Bremerton/Puget Sound	2	**Total (14 Institutions)**	**44**
Kaiser NCORP	2		

C70807 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

The Men's Eating and Living (MEAL) Study: A Randomized Trial of Diet to Alter Disease Progression in Prostate Cancer Patients on Active Surveillance

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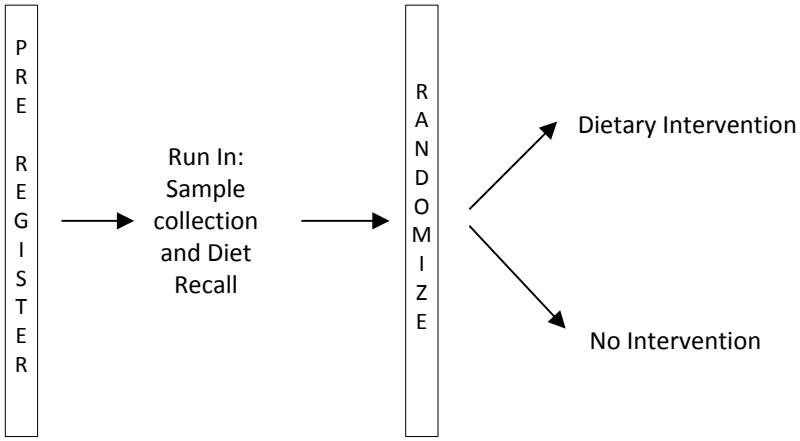
Participants:
Alliance, CTSU

Date Activated:
01/21/2011

Study Chairs:
J Parsons (Alliance), P Van Veldhuizen (SWOG)

SCHEMA



Objectives

To determine if a telephone-based dietary intervention compared to no intervention will decrease clinical progression in active surveillance (AS) patients.

To compare the incidence of active treatment (surgery, irradiation, local ablation, or androgen deprivation) in AS patients receiving dietary intervention compared to no intervention.

To compare prostate cancer-related anxiety in AS patients receiving dietary intervention compared to no intervention.

To compare health-related quality of life in AS patients receiving dietary intervention compared to no intervention.

Patient Population

Patients must have biopsy-proven (consisting of 10 or more tissue cores) adenocarcinoma of the prostate diagnosed within 24 months prior to pre-registration, with less than 25% of the cores positive for cancer, and no more than 50% of any one biopsy tissue core positive for cancer. Patients must have clinical stage less than or equal to T2a and must not have distant metastases. For men less than or equal to 70 years old, biopsy Gleason score must be less than or equal

to 6. For men greater than 70 years old, biopsy Gleason score must by less than or equal to 7 (3 + 4). Baseline serum PSA must be less than 10 ng/ml.

Patients must not have received prior treatment for prostate cancer by surgery, irradiation, local ablative, or androgen deprivation therapy. Patients must not have received treatment with 5-alpha reductase inhibitors within 90 days prior to pre-registration.

Patients must be men aged 50 to 80 years and be able to read and comprehend English language text and be able to understand spoken English over the phone. Patients must not be currently taking coumadin or vitamin supplements including lycopene and beta-carotene.

Patients are eligible for randomization after successful completion of three 24-hour dietary recalls during the run-in period, provided they are not consuming six or more servings per day of fruits and vegetables (not including juices).

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) age: men ≤ 70 years vs men >70 years; (2) race: Black or African American vs other; and (3) baseline prostate biopsy: 0-12 months prior to pre-registration vs >12-24 months prior to pre-registration.

Cancer Control Credits

No cancer control credits are awarded for this study.

Accrual Goals

The accrual goal is 464 patients (232 per arm). Interim analysis will be performed after 80 patients progress or complete the two years of follow-up and then every six months until full information.

Summary Statement

Alliance reported a total accrual of 401 patients as of December 31, 2014, including 134 CTSU registrations from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Madigan Army Med Ctr/Brooke Army Med Ctr	23	San Antonio, U of TX	3
Colorado, U of	17	Stormont-Vail Health/Kansas, U of	3
Virginia Mason CCOP	13	Cleveland Clinic OH	2
Utah, U of	12	Gulf South MU-NCORP	2
Rochester, Univ of	11	Loma Linda Univ	2
Kansas, U of	8	VAMC-West Haven/Yale University	2
Baylor College	7	Atlanta Reg CCOP	1
Cedars-Sinai Med Ctr	6	KaiserPermanenteSCAL/Kaiser NCORP	1
Beaumont NCORP	5	Loyola University	1
Kentucky, U of	4	Poudre Valley Hosp/Colorado, U of	1
Akron Gen Med Ctr/Cleveland Clinic OH	3	St Mary Med Ctr/Puget Sound	1
Bay Area Hospital/Puget Sound	3	**Total (24 Institutions)**	**134**
Heartland NCORP	3		

C90203 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Randomized Phase III Study of Neo-Adjuvant Docetaxel and Androgen Deprivation Prior to Radical Prostatectomy Versus Immediate Radical Prostatectomy in Patients with High-Risk, Clinically Localized Prostate Cancer

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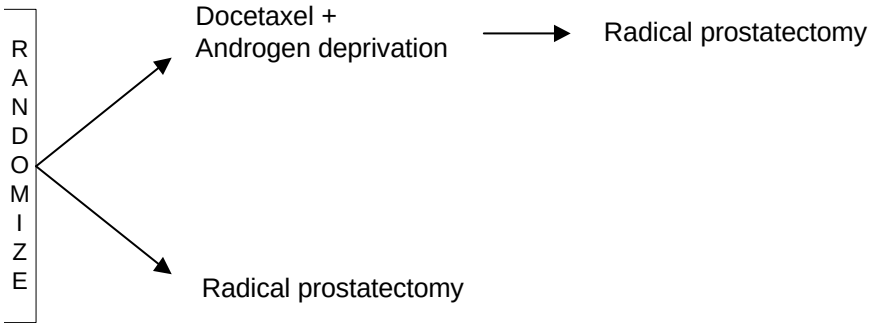
Participants:
Alliance, CTSU

Date Activated:
07/01/2007

Study Chairs:
J Eastham (Alliance), F Kim (SWOG)

SCHEMA



Objectives

To determine whether treatment with neoadjuvant docetaxel and androgen deprivation therapy prior to radical prostatectomy will increase the rate of three-year biochemical progression-free survival (bPFS) compared to treatment with immediate radical prostatectomy alone for high-risk prostate cancer patients.

To compare the five-year bPFS rate, bPFS, disease progression, disease-free survival, and overall survival of patients randomized to the two arms of this trial.

To determine the safety and tolerability of neoadjuvant docetaxel and androgen deprivation therapy prior to surgery for high-risk patients undergoing radical prostatectomy.

To compare the impact of neoadjuvant docetaxel and androgen deprivation therapy on time to clinically apparent local disease recurrence and metastatic disease in high-risk patients undergoing radical prostatectomy for clinically localized prostate cancer.

To compare the impact of neoadjuvant docetaxel and androgen deprivation therapy relative to radical

prostatectomy on pathologic tumor stage, frequency of lymph node metastases, and positive margin rates for high-risk patients undergoing radical prostatectomy for clinically localized prostate cancer.

To determine if changes in serum testosterone levels will predict bPFS.

To determine prospectively whether PSA doubling time (PSADT) is a surrogate endpoint for time to clinical metastases and overall survival.

To evaluate associations between post-diagnosis diet and lifestyle, change in food group intake, and risk of prostate cancer recurrence, independent of treatment.

To identify novel protein expression patterns in serum that predict three-year and five-year bPFS rates in high-risk, clinically localized prostate cancer patients.

To identify novel protein expression patterns in serum that predict biochemical response to neo-adjuvant chemotherapy and androgen deprivation therapy.

To determine if immunohistochemical staining profiles of primary tumors can predict three-year and five-year bPFS rates in high-risk, clinically localized prostate cancer.

To determine whether immunohistochemical staining profiles of primary tumors can predict biochemical response to neoadjuvant chemotherapy and androgen deprivation therapy.

To determine if genes identified during RNA expression analysis as being correlated with recurrence have protein expression that correlates with outcome.

Patient Population

Patients must have histologic documentation of stage T1-T3a prostatic adenocarcinoma. Patients must not have small cell, neuroendocrine, or transitional cell carcinoma. Patients must not have metastatic disease as demonstrated by negative biopsy in pelvic lymph nodes > 1.5 cm and negative bone scan. The Kattan nomogram predicted probability of being free from biochemical progression at five years after surgery must be <60% or Gleason sum = 8.

Patients must not have any prior treatment for prostate cancer including surgery (excluding TURP), pelvic lymph node dissection, radiation therapy, or chemotherapy. Patients may have received up to four months of androgen deprivation therapy (LHRH agonists, antiandrogens, or both) prior to being enrolled on this study.

Patients must have an ECOG performance status of 0-2 and have adequate renal, hepatic, and hematologic function. Prestudy PSA must be ≤ 100 ng/mL.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) nomogram-predicted biochemical progression-free survival at five years: 0%-20.9% vs 21%-39.9% vs 40%-59.9% vs ≥ 60%; and (2) androgen deprivation therapy prior to randomization (≤ 4 months): yes vs no.

Cancer Control Credits

No cancer control credits are awarded for this study.

Accrual Goals

The accrual goal for this study is 750 patients (375 per arm). Interim analyses will be performed when the percentage of men with at least three years of follow-up reaches the following points: 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 100%.

Summary Statement

Alliance reported a total accrual of 692 patients as of December 31, 2014, including 145 CTSU registrations from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Davis, U of CA	40	H Lee Moffitt CC	2
Colorado, U of	15	Heartland NCORP	2
Kansas, U of	13	Michigan CRC NCORP	2
City of Hope Med Ctr	10	Quad Cities/Genesis/Loyola University	2
Loyola University	10	Rochester, Univ of	2
Virginia Mason CCOP	10	Henry Ford Hosp	1
Irvine, U of CA	5	LSU-Shreveport/Gulf South MU-NCORP	1
VAMC-West Haven/Yale University	5	Mississippi, Univ of	1
Madigan Army Med Ctr/Brooke Army Med Ctr	4	New Mexico MU-NCORP	1
So Calif, U of	4	Oregon Hlth Sci Univ	1
Wayne State Univ	4	Rockwood Clinic, PS/Puget Sound	1
MD Anderson	3	Sutter Cancer RC	1
Upstate Carolina	3	**Total (26 Institutions)**	**145**
Gulf South MU-NCORP	2		

C90601 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Randomized Double-Blinded, Placebo-Controlled Phase III Study Comparing Gemcitabine, Cisplatin, and Bevacizumab to Gemcitabine, Cisplatin, and Placebo in Patients with Advanced Transitional Cell Carcinoma

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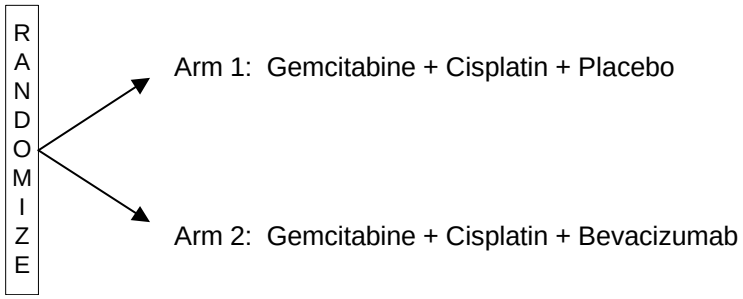
Participants:
Alliance, CTSU

Date Activated:
08/15/2009

Study Chairs:
J Rosenberg (Alliance), T Flaig (SWOG)

Date Closed:
12/02/2014

SCHEMA



Objectives

To determine if patients with advanced transitional cell carcinoma treated with bevacizumab, gemcitabine and cisplatin will have increased overall survival when compared to patients treated with gemcitabine, cisplatin, and placebo.

To compare the progression-free survival of these two regimens in patients with advanced transitional cell carcinoma.

To compare the proportion of patients who experience an objective response on each regimen.

To compare Grade 3 and greater toxicities in patients treated on the two regimens.

Patient Population

Patients must have histologically or cytologically documented metastatic or unresectable transitional cell (urothelial) carcinoma of the urinary tract (renal pelvis, ureter, bladder, prostate, or urethra), with metastatic or locally advanced disease (T4b, N2, N3, or M1). Patients must not be candidates for potentially curative surgery or radiotherapy. Patients must not have known history of brain metastases.

Patients must not have received combination systemic chemotherapy for metastatic disease. Radiosensitizing single agent is not considered prior systemic therapy. Prior neoadjuvant or adjuvant systemic chemotherapy is permissible provided the interval from end of therapy to diagnosis of metastatic disease is at least one year. Patients may have received prior radiation (including palliative) or

major surgery provided it was greater than four weeks before registration and the patient is fully recovered. Patients may have received prior intravesical therapy provided it was greater than four weeks before registration. Patients must not have had prior treatment with bevacizumab or other angiogenesis inhibitors.

Patients must have ECOG performance status 0-1 and be at least 18 years of age. Patients must not have current congestive heart failure or uncontrolled hypertension. Patients must not have a significant history of bleeding, GI perforation, or peritoneal carcinomatosis. Patients must not have had an arterial thrombotic event within six months of registration. Patients who have experienced a deep venous thrombosis or pulmonary embolus within six months prior to registration must be on stable therapeutic anticoagulation medication. Patients must not have sensory or motor peripheral neuropathy greater than or equal to Grade 2. Patients must not have known hypersensitivity to Chinese hamster ovary cell products.

Stratification/Descriptive Factors

Patients will be stratified according to the following factors: (1) presence of visceral metastases (defined as lung, liver, bone, splenic, or intra-abdominal metastases): yes vs no: and (2) prior chemotherapy for treatment of TCC (including adjuvant, neo-adjuvant, and single agent radiosensitizers): yes vs no.

Accrual Goals

The accrual goal of this study is 500 patients (250 per arm). Interim analyses will be performed when the total number of deaths reaches 125, 182, 244, 302, 347, 382, 405, and 445.

Summary Statement

This study was permanently closed to new patient accrual on December 2, 2014 after meeting its accrual goal. A total of 506 patients were registered prior to closure, including 101 CTSU registrations from SWOG institutions. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Colorado, U of	15	Loyola University	2
Cleveland Clinic OH	8	NE Georgia Med Ctr/Mississippi, Univ of	2
Wichita NCORP	8	Northwest CCOP	2
So Calif, U of	7	Puget Sound	2
Baylor College	4	St Louis CCOP	2
Kentucky, U of	4	Sutter Cancer RC	2
MUSC MU-NCORP	4	Arizona MC, U of	1
Columbus NCORP	3	Arkansas, U of	1
Henry Ford Hosp	3	Michigan CRC NCORP	1
KaiserPermanenteCOL/Kaiser NCORP	3	Montana NCORP	1
Kansas, U of	3	Orange Reg Med Ctr/Columbia University	1
UF Cancer Center/Arkansas, U of	3	Poudre Valley Hosp/Colorado, U of	1
Upstate Carolina	3	Rochester, Univ of	1
Yale University	3	St Elizabeth's MC/Davis, U of CA	1
Atlanta Reg CCOP	2	St Luke's Mt State	1
Columbia University	2	Virginia Mason CCOP	1
Heartland NCORP	2	**Total (34 Institutions)**	**101**
Irvine, U of CA	2		

E2810 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Randomized, Double-Blind Phase III Study of Pazopanib vs Placebo in Patients with Metastatic Renal Cell Carcinoma Who Have No Evidence of Disease Following Metastatectomy

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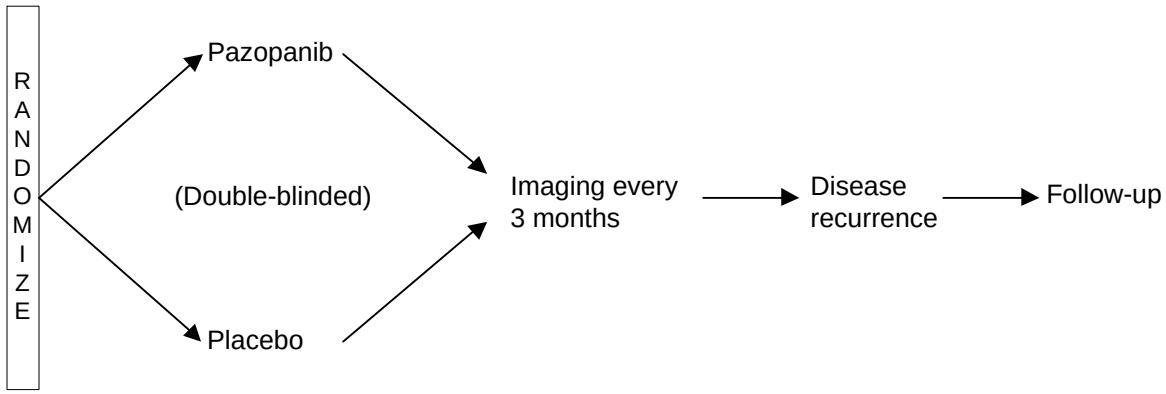
Participants:
ECOG-ACRIN, CTSU

Date Activated:
04/17/2012

Study Chairs:
L Appleman (ECOG-ACRIN), S Pal (SWOG)

SCHEMA



Objectives

To evaluate disease-free survival of patient with renal cell carcinoma (RCC) treated with pazopanib as compared to placebo.

To describe the overall survival of patients with advanced RCC randomly assigned to receive placebo or pazopanib for one year following metastatectomy to NED.

To describe treatment- and (at recurrence) disease-related adverse events in the two treatment arms.

To analyze quality-adjusted time without symptoms of disease or treatment (Q-TWiST) for subjects in the two treatment arms.

To characterize changes in patient-reported fatigue and (at recurrence) kidney cancer-related symptoms during and following treatment with pazopanib compared to placebo.

To explore the association between plasma trough levels of pazopanib and disease-free and overall survival.

To prospectively bank preserved tissue from primary tumors and associated metastatic sites in patients with RCC.

Patient Population

Patients must have pathologically confirmed renal cell carcinoma with a clear cell component. Pure papillary and chromophobe histologies are excluded.

Patients must have undergone nephrectomy or partial nephrectomy to remove primary renal cell carcinoma. Patients must have undergone surgical resection to remove one or more sites of metastatic disease, with successful removal of all known sites two to twelve weeks prior to randomization. Eligible patients must have no evidence of disease on post-operative imaging. Patients must not have received any prior or concurrent systemic therapy for RCC; prior adjuvant placebo administration is permitted. Patients cannot be taking strong CYP3A4 inhibitors. Patients must not be taking drugs known to prolong the QTc interval; such drugs should be discontinued at least one week prior to randomization.

Patients must have ECOG performance status of 0 or 1 and adequate hematologic, renal, hepatic, and cardiac function. Patients must have no uncontrolled intercurrent illness. Patients must have no history of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess, myocardial infarction, cerebrovascular accident (CVA), hospital admission for unstable angina, cardiac angioplasty, or stenting, venous thrombosis, or hemoptysis in excess of 2.5 mL.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) disease-free interval: $\leq$ 1 year vs > 1 year; and (2) number of sites of metastatic disease resected at metastatectomy: 1 vs >1.

Cancer Control Credits

The NCI Division of Cancer Prevention has not assigned cancer control credits for registration to this study. There are potential cancer control credits for quality of life.

Accrual Goals

The accrual goal for this study is 128 patients (64 per arm). Interim analyses will be performed after 31% information is attained and then every six months until full information.

Summary Statement

ECOG-ACRIN reported a total accrual of 58 patients as of December 31, 2014, including 23 CTSU registrations from SWOG institutions. The complete Spring 2014 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg
City of Hope Med Ctr	10
Kansas, U of	3
Oregon Hlth Sci Univ	3
Utah, U of	3
Columbia Univ NCORP	1
Michigan, U of	1
Southeast CCC NCORP	1
Stormont-Vail Health/Kansas, U of	1
Total (8 Institutions)	**23**